Int J Clin Exp Med 2017;10(4):6853-6860
www.ijcem.com /ISSN:1940-5901/IJCEM0045282

Original Article

Ultrasonic scalpel treatment for HIV positive patients with giant cell tumor of long bone

Sheng Sun[1*], Yao-Shen Zhang[2*], Qiang Zhang[1], Chang-Song Zhao[1], Xin Li[1], Ru-Gang Zhao[1], Jing-Jing Wang[1]

[1]Department of Orthopedics, Beijing Ditan Hospital, Capital Medical University, Beijing 100015, China; [2]Department of Orthopedics, Beijing Chaoyang Hospital, Capital Medical University, Beijing 100015, China. [*]Equal contributors.

Received October 15, 2016; Accepted February 13, 2017; Epub April 15, 2017; Published April 30, 2017

Abstract: Giant cell tumor (GCT) is a kind of osteolytic tumor, mononuclear cells and osteoclasts multiple nuclear cells as the main component, strong local invasiveness, high recurrence rate are its main clinical features. Human immunodeficiency virus (HIV) infection leads to a decrease of the count of CD4 T-cell, and the dysfunction of the macrophages and monocytes. As we know, there were few literature about HIV positive patients with GCT, and there is no effective treatment of this disease currently. In this research, treatment for HIV positive patients with GCT and some follow-up results was discussed. This research retrospectively analyzed 7 HIV positive patients with GCT, 4 male patients and 3 female patients, with a age range 31 to 65 years old (45.4 years old on average) were included. From March 2008 to February 2015, curettage by ultrasonic scalpel burr were performed in 7 patients, combined with local methotrexae gelfoam adjuvant treatment, and then filled with allograft and/or homograft bone. All patients were followed up for 2 years. No local recurrence and pulmonary metastases was observed. After treatment, all 7 patients showed good bone knitting and rehabilitation without deformity and functional problem. Segmental bone graft was perfectly incorporated with no evidence of significant immune rejection, collapse and fracture, and there were no functional disability after operation. In conclusion, curettage by ultrasonic scalpel burr with local methotrexate gelfoam adjuvant treatment and filled with allograft and/or homograft bone showed satisfactory results in HIV positive patients with GCT. And it was a safe and effective treatment.

Keywords: HIV, GCT, ultrasonic scalpel, burr, curettage, surgical treatment

Introduction

Giant cell tumor (GCT) is a kind of osteolytic tumor, mononuclear cells and osteoclasts multiple nuclear cells as the main component, strong local invasiveness and high recurrence rate were its main clinical features [1, 2]. The treatment of GCT including intralesional curettage and local adjuvant therapies, such as phenol or liquid nitrogen zoledronic acid, have been recommended [3, 4]. Acquired immune deficiency syndrome (AIDS) arises from human immunodeficiency virus (HIV) infection. HIV infection leads to a decrease of the count of CD4 T-cell, and the dysfunction of the macrophages and monocytes. It finally leads to immunodeficiency [5, 6]. Further questions to be asked are, whether HIV patients are more likely to have giant cell tumors of bone? Is there a higher rate of recurrence and metastasis about HIV infection in patients with GCT? How does it responds to treatment? However, at present, few literatures reported about HIV positive patients with GCT and there are no effective treatments of this disease currently. Ultrasonic scalpels may be used to cut tissue and avoid bleeding simultaneously [7, 8]. Over the past decade, we have experienced successful treatment of GCT patients with long bones using this technique in our hospital [9, 10].

In this study, we reported the application of ultrasonic scalpel treatment in HIV positive patients with giant cell tumor of bone, and we also tried to find out its advantages and curative effects.

Methods

Patients

From March 2008 to February 2015, 7 HIV positive patients with giant cell tumor of bone were

Table 1. Demographic and HIV-related details

n	Gender distributiong		Age on Admission (yr)	Occurrence site	CD4 T-cell Count on Admission (Absolute/mL)	HIV-RNA (Copies/mL)	HAART	Co-morbidities
	Male	Women						
1	1		46	Distal radius	302	4574	Y	N
2	1		39	Proximal femur	354	< 20	Y	N
3		1	48	Distal femur	465	57	Y	N
4		1	31	Proximal tibia	447	Undetectable	Y	N
5		1	65	Proximal tibia	337	2553	Y	Hypertension
6	1		32	Proximal tibia	386	94	Y	N
7	1		57	Proximal humerus	573	Undetectable	Y	Diabetes mellitus

admitted to our hospital, 4 male patients and 3 female patients were included. HIV infection was confirmed by enzyme-linked immunosorbent assay (ELISA) and Western blotting. All patients also had their viral load measured (VL). The age range was 31 to 65 years old (average 45.4 years old). Highly active antiretroviral therapy (HAART, including Tenofovir disoproxil + Lamividine + Efavirenz) was performed in all patients and 750 mg of cefuroxime/8 h were given from the day of operation to 10 days after. Intravenous or oral amino acids, albumin injection, and thymopentin were administered as routine nutritional supplementation to improve nutrition and hypoalbuminemia. Infusions of red blood cell suspension and/or plasma were administered as necessary. Occurrence site: distal radius 1 cases, distal femur 1 cases, proximal femur 1 case, proximal tibia 3 cases, proximal humerus 1 case (**Table 1**). Curettage by Ultrasonic scalpel burr was performed in all patients, combined with local methotrexate gelfoam adjuvant treatment, and then filled with allograft and/or homograft bone. Plain radiographs, chest X-ray, computed tomography (CT) and/or magnetic resonance imaging (MRI) were performed in more than one plane. Fine needle aspiration cytology (FNAC) and/or open biopsy were performed in all patients. Thickness of the subchondral bone at the adjacent articular surface was measured. Clinical and radiographic examinations were performed regularly in the follow-up period. Examinations were performed at 1, 3 and/or 6 months after operation and then after every 6 months for 3 years. After that, no further follow-up examination was routinely scheduled. Patients who did not experience recurrence were censored at the last follow-up study, and the mean period of follow-up was 24 (12-36) months. Clinical examination and conventional radiography at the operative site were included in the routine follow-up study. CT and MR imaging was used for further investigation when radiography demonstrated a suspected relapse (such as graft or bone resorption, expansile change and local soft tissue swelling/mass formation, etc.) or when clinical symptoms and signs showed recurrence even the radiography were negative. In addition, a plain radiograph or CT of the chest was performed to exclude metastasis.

Surgery

For HIV positive patients with primary GCTs, our preferred treatment was to c arry out curettage in the lesion with high-speed ultrasonic scalpel, bur the tumor cavity to improve the thoroughness of tumor resection, and then combined with local methotrexate gelfoam adjuvant treatment and filled with allograft and/or homograft bone. Sufficient fenestration as well as repeatedly grind and scratch on the tumor chamber wall was necessary until tumor tissue was completely cleared away in the naked eyesight. We carefully retained the normal bone and epiphysial bone lamella. After that, we rinsed repeatedly with physiological saline and then methotrexate regional chemotherapy with methotrexate-gelatin sponge were applied. During bone grafting, we measured the size of the bone cavity and the autogenous iliac bone were taken. If the bone cavity was too large, we would use the allogeneic freeze-dried bone (Osteolink Biomaterial Co., Ltd., Hubei, China) to mix filling (**Figure 1A**, **1B**). Occupational exposure protection (**Figure 2**): to avoid occupational exposure, surgeons were equipped with waterproof gowns, caps, masks, a pair of

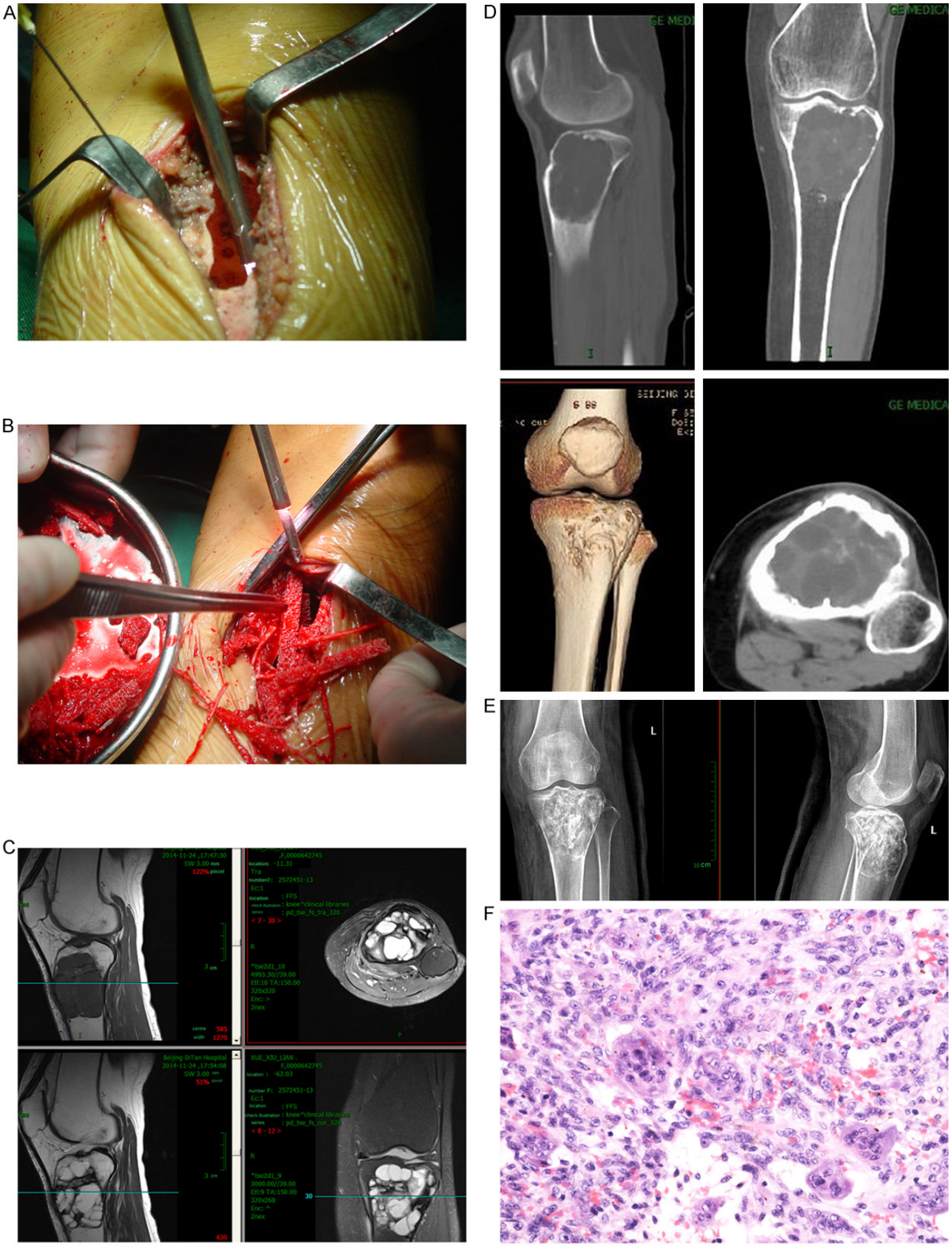


Figure 1. A. Sufficient fenestration as well as repeatedly grind and scratch on the tumor chamber wall was necessary until tumor tissue was completely cleared away in the naked eyesight during operation. We carefully reserved the normal bone and epiphysial bone lamella. B. Filled with allograft and/or homograft bone in during operation. C. November 2012, a 65-year-old female complained of pain left and claudication for 3 months. She diagnosed with left the proximal tibia bone giant cell tumors and HIV infection in the left the proximal tibia bone giant cell tumors, Preoperation MRI imaging findings. D. Radiographs show the preoperation situation: the tumor decenter growth, large erosion extent, multilocular, cortical bone expansion and thinning. E. After 15 months later, tumor resection radiographs (lateral radiograph) show left the proximal tibia bone after ultrasonic scalpel burr curettage, combined with local methotrexate gelfoam adjuvant treatment and filled with allograft and/or homograft bone. No local recurrences. The bone is filled and healed well. Left the proximal tibia has no collapse or fracture at final 15 months follow-up study. F. Pathological examination indicates cystic and necrosis.

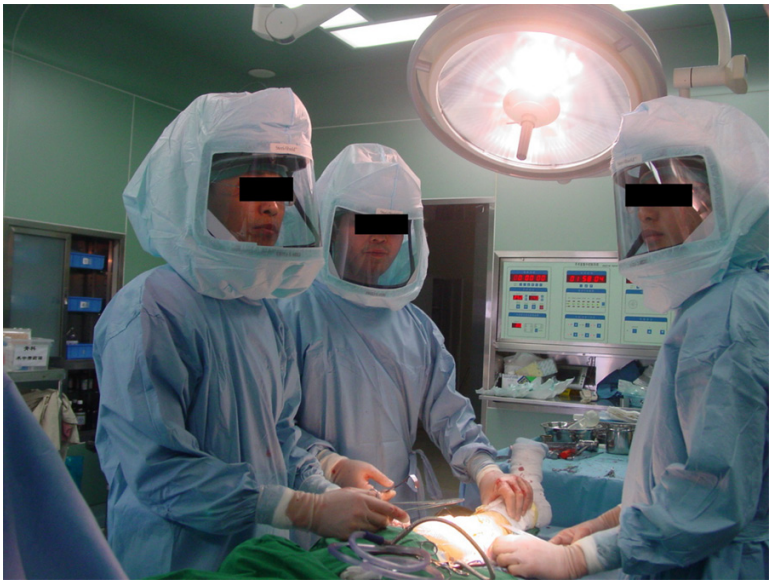


Figure 2. To prevent occupational exposure equipment in surgery.

powder-free synthetic surgical gloves (G-VIR, HUTCHINSON SANTE S.N.C, 2, Ruo Balzac-75063 Pairs, France), and protective boots. Ultrasonic scalpel burring of the tumor cavity was performed in the patients, to improve the thoroughness of tumor resection, and then local methotrexate gelfoam adjuvant treatment were performed and filled with allograft and/or homograft bone. There was no rejection reaction and bone resorption phenomenon in both autogenous iliac bone and allogeneic freeze-dried bone mixed filling in all patients.

Ultrasonic scalpel devices: "EXPLOITER" Ultrasonic Scalpel was purchased from Beijing Beyonder Technologies Co., Ltd. (Exploiter TM UOSS-II). The device is made up of three parts: the main engine, hand shank and burring, cooling system. Working principle: signal generator is controlled by the ultrasonic frequency electrical signal from the computer. After amplified by the power amplifier, the electrical signal drives ultrasonic transducer. Then the ultrasonic transducer produces vibratory motion. Ultrasonic amplitude transformer amplifies the amplitude and drives the cutter to work. Operational frequency is 40±2 kHz. Real-time automatic frequency tracking was performed. Cutter's amplitude < 300 μm. We equipped 3 mm and 2 mm burr with cutting tooth and notched burr, which were suitable for different needs of burring. We set the ultrasonic energy output to 30%. The handle was equipped with the cooling system. Cutting tools could take the clockwise or anti-clockwise and reciprocal rotation alternately to increase the burring ability [8, 10].

Results

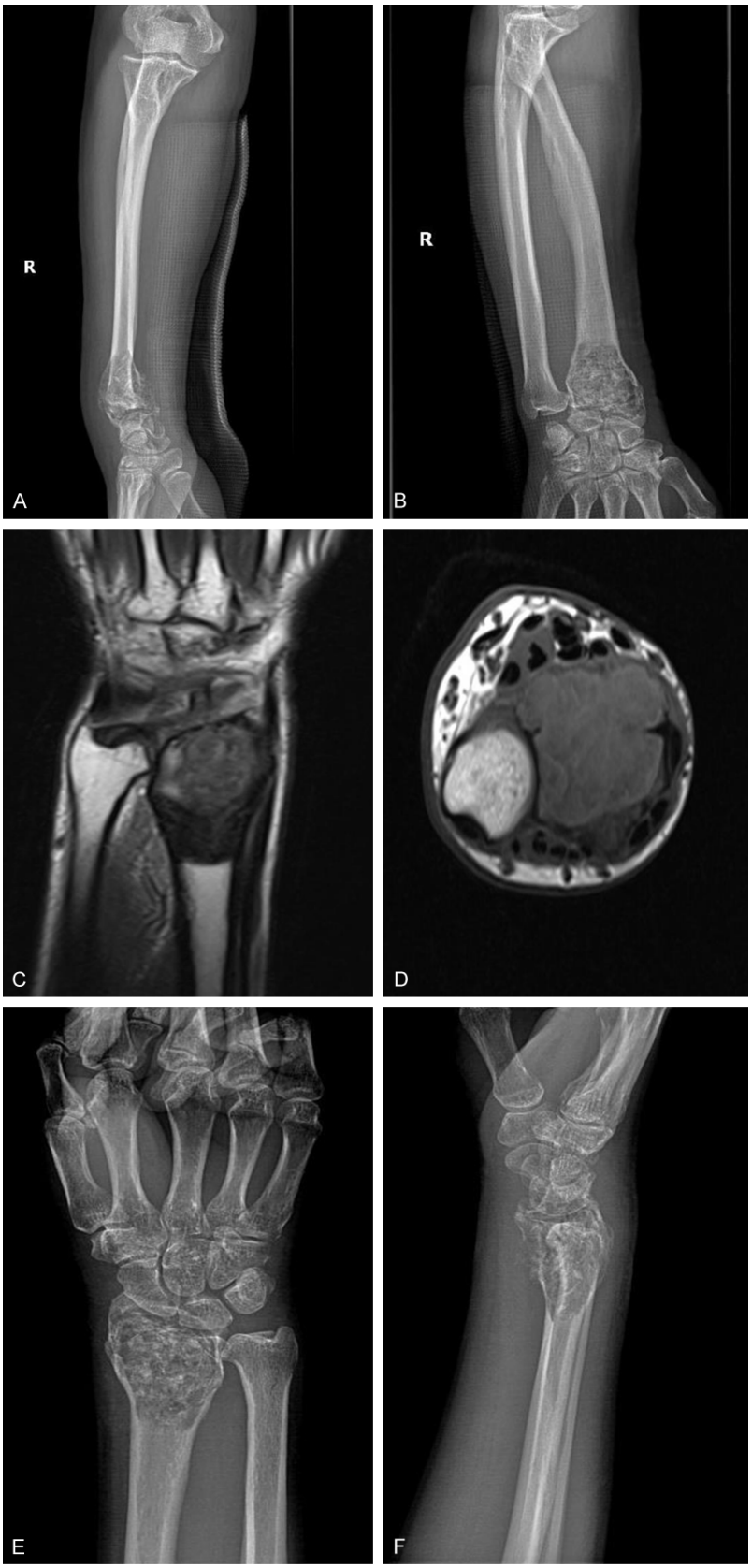
HIV transmission routes including blood product transfusion, intravenous drug use, and unprotected sex. The patients had been diagnosed with HIV at a mean time of 4.3 years before surgery. Viral load and CD4 T-cell count were available for all HIV-positive patients. The mean HIV RNA level was 1043 copies/mL. The mean CD4 T-cell count was 409 cells/mm^3.

All patients were taking highly active antiretroviral therapy (HAART) at the time of surgery. There were no complications such as DVT, early sepsis or late sepsis. There was no mortality due to AIDS related complications. All incisions achieved primary healing. Operations were performed successfully without occupational exposure.

Allograft reconstruction was perfect. During the 24 months of follow-up after the operation, local recurrence of the tumor and distant metastasis were not found. All patients had good bone knitting. No phsical deformities, partial collapse, fracture, obvious function obstacle and rejection was found, and there was no distant metastasis. The typical cases were showed in the **Figures 1C-F**, **3A-G**.

Discussion

HIV infection leads to a reduction of CD4 T-cell counts, dysfunction of the macrophages and monocytes, and thus finally leads to immunodeficiency [11]. Kaposi's sarcoma and B-cell lymphomas develop specific morbidity and behavioral biology in a more radical manner than which is generally seen in population at large [12]. Chronic inflammation is a well-established risk factor for bone loss. Bone resorption occurs through osteoclasts, highly special-



ized cells formed from the fusion of the origin of monocyte/macrophage cells [13, 14]. In inflammatory conditions, RANKL is also expressed by activated T-cells and B-cells, resulting in increased osteoclast activity and bone loss. Given that increased inflammation, T-cell activation, and monocyte activation contribute to the pathogenesis of many HIV-related comorbidities [15]. We hypothesized that normal host containment of this neoplasm (GCT) would be associated with increased inflammation, T-cell activation, and monocyte activation among HIV-infected persons on stable highly active antiretroviral therapy (HAART). At present, local adjuvant treatment including hyperthermia (microwave, electricity), cryotherapy (liquid nitrogen), chemical reagent daub or soak (phenol, liquid nitrogen, carbolic acid, alcohol, 50% zinc chloride, hydrogen peroxide, zoledronic acid, etc). Moreover, high-speed abrasive drilling and pulse rinse can clean the tumor tissue well [15-20]. The ultrasonic scalpel burr has developed rapidly in recent years. And owing to its selective fragmentation, little injury, high accuracy and the unique advantages such as avoiding bleeding, it has been applied in orthopedics [21]. However, the use of ultrasonic scalpel in treatment of HIV positive combined with GCT of bone has never been reported.

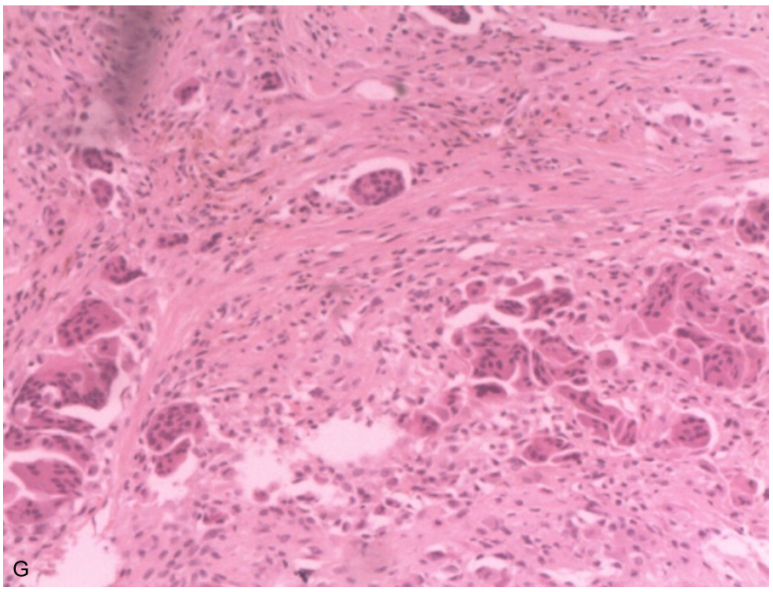


Figure 3. A, B. A 46 years old male patients, right of giant cell tumor of the distal part of the radius, HIV (+), viral load 4574 copies/ul. CD4+ T lymphocyte count was 302 cells/ul preoperation. Radiographs show the preoperation situation: the tumor decenter growth, large erosion extent, multilocular, cortical bone expansion and thinning. C, D. Preoperation MRI imaging showing a radiolucent, expansile, lytic lesion in right the proximal the distal part of the radius. E, F. After 24 months later, tumor resection radiographs show distal radius bone after ultrasonic scalpel burr curettage and combined with local methotrexate gelfoam adjuvant treatment and filled with allograft and/or homograft bone. No local recurrences. The bone is filled and healed well. Distal radius has no pain or fracture at final 24 months follow-up study. G. Pathological examination indicates cystic and necrosis.

Follow-up study

HIV infected patients had low immunity. In clinical practice, CD4+ lymphocyte count was related with the risk classification of HIV infected patients [22, 23]. When CD4+ T lymphocyte count was greater than 2, mortality and morbidity increased significantly. Although, its significance was still questionable, not all studies had proved it [24]. There were no clinical complications (wound infection, bone infection, incision exudation and delayed healing) in our patients. Our patients had received highly active antiretroviral therapy (HAART) for 1 year and viral load was low, so there was no immunosuppression to show the occurrence of systemic metastases.

The effect of burring and damaging the tumor tissue is more ideal. Ultrasonic scalpel burr makes surgery more safer. Ultrasonic scalpel burr's working temperature is 70-80°C, which is enough to destroy the tumor cells. In addition, the surface of the wound and the bone graft by the operation heals more faster. When ultrasonic scalpel burr is working, the suitable temperature can promote hemoglobin's solidification, render simultaneous homeostasis. Compared with the electric cutting and coagulation, there are less smoke, no eschar and more clear surgical field. Ultrasonic scalpel burr has its unique property, which is the separation, hemostasis and cutting can work together in one machine. It could destroy and remove the tumor more completely, and without any damage of the normal tissue. According to its safety, easy control and good application effect, ultrasonic scalpel burr has a good application prospect.

Conclusion

In our opinion, for the treatment of GCT, ultrasonic scalpel is mainly based on its fragmentation and the cavitation effect. These two functions can thoroughly clean the tumor cavity tissue even in the depth of normal bone, remove tumors source completely, and then create a very good bone graft bed. The bone have knitted well, and there was no tumor recurrence and metastasis currently. And it avoids the traditional treatment's shortage: tumor tissue cannot be removed thoroughly; the normal bone can be necrosis; the normal bone healing is always delayed. There were no recurrence in our patients with 24 months follow-up study. The recent efficacy is good, safe and effective of the application of ultrasonic scalpel tumor curettage and local chemotherapy and autologous or allogeneic bone transplantation in treatment of those HIV positive patients with primary GCT. HIV infection merged in patients with GCT are not more likely to relapse after the operation in this research. And the limitation of this study is the sample size was not enough and the follow-up time was short, so the clinical curative effect remains to be studied further.

Acknowledgements

The medical science and technology promotion project of Beijing Municipal Commission of Health and Family Planning. Project number: TG-2015-05. The National Clinical Key Department of Infection Diseases; National Major Scientific and Technological Project (No.2014-ZX10005002-002).

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Qiang Zhang, Department of Orthopedics, Beijing Ditan Hospital, Capital Medical University, No. 8, Jingshun East Street, Chaoyang District, Beijing 100015, China. Tel: +86-10-13718271838; Fax: +86-10-84322491; E-mail: qiangzhang12@126.com

References

[1] Chakarun CJ, Forrester DM, Gottsegen CJ, Patel DB, White EA and Matcuk GR Jr. Giant cell tumor of bone: review, mimics, and new developments in treatment. Radiographics 2013; 33: 197-211.

[2] Yip KM, Leung PC and Kumta SM. Giant cell tumor of bone. Clin Orthop Relat Res 1996; 60-64.

[3] Nishisho T, Hanaoka N, Endo K, Takahashi M and Yasui N. Locally administered zoledronic Acid therapy for giant cell tumor of bone. Orthopedics 2011; 34: e312-315.

[4] Klenke FM, Wenger DE, Inwards CY, Rose PS andSim FH. Recurrent giant cell tumor of long bones: analysis of surgical management. Clin Orthop Relat Res 2011; 469: 1181-1187.

[5] Zapata HJ and Shaw AC. Aging of the human innate immune system in HIV infection. Curr Opin Immunol 2014; 29: 127-136.

[6] Abalo A, Patassi A, James YE, Walla A, Sangare A and Dossim A. Risk factors for surgical wound infection in HIV-positive patients undergoing surgery for orthopaedic trauma. J Orthop Surg (Hong Kong) 2010; 18: 224-227.

[7] Tian W, Shi W, Zhou Z and Luo X. The use of Ultrasonic Scalpel in the spinal surgery. Chinese Journal of Spine and Spinal Cord 2005; 15: 753-757.

[8] Amaral JF. Laparoscopic cholecystectomy in 200 consecutive patients using an ultrasonically activated scalpel. Surg Laparosc Endosc 1995; 5: 255-262.

[9] Zhang Q, Zou D, Ma H and Hai Y. Application of ultrasonic scalpel in treatment of giant cell tumor of the long bones. Orthopedic Journal of China 2007; 15: 1181-1183.

[10] Sun S, Zhang Q, Zhao CS and Cai J. Long-term outcomes of ultrasonic scalpel treatment in giant cell tumor of long bones. Oncol Lett 2014; 8: 145-150.

[11] Sobottke R, Zarghooni K, Krengel M, Delank S, Seifert H, Fatkenheuer G, Ernestus I, Kallicke T, Frangen T, Arasteh K, Oette M and Eysel P. Treatment of spondylodiscitis in human immunodeficiency virus-infected patients: a comparison of conservative and operative therapy. Spine (Phila Pa 1976) 2009; 34: E452-458.

[12] List AF. Metastatic giant-cell bone tumor in a man positive for HIV. N Engl J Med 1988; 318: 517.

[13] O'Brien CA. Control of RANKL gene expression. Bone 2010; 46: 911-919.

[14] Kawai T, Matsuyama T, Hosokawa Y, Makihira S, Seki M, Karimbux NY, Goncalves RB, Valverde P, Dibart S, Li YP, Miranda LA, Ernst CW, Izumi Y and Taubman MA. B and T lymphocytes are the primary sources of RANKL in the bone resorptive lesion of periodontal disease. Am J Pathol 2006; 169: 987-998.

[15] Ofotokun I, McIntosh E and Weitzmann MN. HIV: inflammation and bone. Curr HIV/AIDS Rep 2012; 9: 16-25.

[16] Messoudi A, Fnini S, Benjeddi Y, Sirajelhak M, Bouyarmanne H, Arssi M and Largab A. [Giant cell tumors of the distal radius: resection: reconstruction by long avascular fibular graft (a case report)]. Chir Main 2011; 30: 345-348.

[17] Zhen W, Yaotian H, Songjian L, Ge L and Qingliang W. Giant-cell tumour of bone. The long-term results of treatment by curettage and bone graft. J Bone Joint Surg Br 2004; 86: 212-216.

[18] Vult von Steyern F, Bauer HC, Trovik C, Kivioja A, Bergh P, Holmberg Jorgensen P, Folleras G, Rydholm A; Scandinavian Sarcoma Group. Treatment of local recurrences of giant cell tumour in long bones after curettage and cementing. A Scandinavian sarcoma group study. J Bone Joint Surg Br 2006; 88: 531-535.

[19] Sakayama K, Sugawara Y, Kidani T, Miyawaki J, Fujibuchi T, Kamei S, Aizawa J and Yamamoto H. Diagnostic and therapeutic problems of giant cell tumor in the proximal femur. Arch Orthop Trauma Surg 2007; 127: 867-872.

[20] Hoch B, Inwards C, Sundaram M and Rosenberg AE. Multicentric giant cell tumor of bone. Clinicopathologic analysis of thirty cases. J Bone Joint Surg Am 2006; 88: 1998-2008.

[21] Al-Mahfoudh R, Qattan E, Ellenbogen JR, Wilby M, Barrett C and Pigott T. Applications of the ultrasonic bone cutter in spinal surgery-our preliminary experience. Br J Neurosurg 2014; 28: 56-60.

[22] Norrish AR, Lewis CP and Harrison WJ. Pin-track infection in HIV-positive and HIV-negative

patients with open fractures treated by external fixation: a prospective, blinded, case-controlled study. J Bone Joint Surg Br 2007; 89: 790-793.

[23] Huang WC, Kwon EO, Scardino PT and Eastham JA. Radical prostatectomy in patients infected with human immunodeficiency virus. BJU Int 2006; 98: 303-307.

[24] Harrison WJ, Lewis CP and Lavy CB. Wound healing after implant surgery in HIV-positive patients. J Bone Joint Surg Br 2002; 84: 802-806.