Orthopaedics & Traumatology: Surgery & Research 106 (2020) 813–818

Contents lists available at ScienceDirect

Orthopaedics & Traumatology: Surgery & Research

journal homepage: www.elsevier.com

Original article

Outcome of Induced Membrane Technique in Treatment of failed previously operated Congenital Pseudarthrosis of the Tibia

Mohammed Anter Meselhy*, Adel Samy Elhammady, Mohamed Salah Singer

Orthopedic Department, Benha University, Kafer el gazar, Benha, 13511 Qalyubia, Egypt

ARTICLE INFO

Article history:
Received 5 July 2019
Accepted 20 November 2019

Keywords:
Congenital pseudarthrosis of the tibia
Induced membrane technique
Ilizarov circular fixator
Free non vascularised fibular graft
Masquelet technique

ABSTRACT

Background: Although a remarkable success in the treatment of congenital pseudarthrosis tibia (CPT) had been achieved, failure rate is still high and the likelihood of amputation is still considerable. The current study evaluates the outcome of induced membrane technique in the treatment of failed previously operated patients of congenital pseudarthrosis of the tibia. We hypothesized that induced membrane technique will improve union rates in CPT with failed previous multiple operations.
Patients and methods: Nineteen consecutive patients of failed previously operated CPT were prospectively included in the study. All patients were treated by induced membrane technique with autogenous free non-vascularized fibular strut graft augmented by autogenous iliac graft and fixed by intramedullary K-Wire as well as Ilizarov external fixator.
Results: The mean interval between the 1st and 2nd stages of the procedure was 4.9 weeks. Sound union was achieved in all cases in a mean time of 25.3 weeks. The mean follow up period was 5.02 years (range, 2.4-6.5). No refracture was documented till last follow up.
Conclusion: Induced membrane technique had proved as a successful method in the treatment of failed previously operated CPT with a satisfactory outcome and low complication rates.
Level of evidence: IV.

1. Introduction

Congenital pseudarthrosis of the tibia (CPT) is a rare pediatric disorder that represents one of the most challenging conditions in orthopaedic surgery. An association of CPT and type 1 neurofibromatosis always carries a bad predictive sign for bone union [1–3].

Although a remarkable success in treatment of CPT had been achieved by variable techniques (as vascularised fibular graft transfer and bone transport by Ilizarov), multiple surgeries are sometimes necessary, with poor prognosis [1].

Induced membrane technique has been successfully used to treat diaphyseal bone loss in adults and children through putting a bone cement in the defect to induce a biological membrane that was filled by cancellous bone graft [4]. The aim of the current study was to evaluates the outcome of the induced membrane technique in the management of congenital pseudarthrosis of the tibia with failed previous multiple surgeries. We hypothesized that induced membrane technique will improve union rates in CPT with failed previous multiple operations.

2. Patients and methods

Between January 2010 and February 2016, 19 consecutive patients of congenital pseudarthrosis of the tibia were prospectively enrolled in the current study. The inclusion criteria was patients with CPT after previous unsuccessful surgical procedures, healthy ipsilateral or contralateral fibula. All patients were treated by induced membrane technique with fixation by Ilizarov frame and intramedullary wire using combined free non vascularised fibular and iliac autograft. The study protocol was authorized by the ethical committee and all patients' legal guards have signed an informative consent.

2.1. Surgical technique

All surgeries were done under general anaesthesia, with the use of pneumatic tourniquet. The site of tibial pseudarthrosis was approached through anterolateral approach. The 1st stage consisted of removal of the hardware if present, radical excision of the pseudarthrosis, the periosteum and refreshing bone ends till reaching bloody healthy bone on both proximal and distal ends with open medullary canal. The length of the bone defect was measured, Ilizarov external fixator was applied. Then gentamicin-loaded bone

* Corresponding author.
E-mail address: m.anteroof@yahoo.com (M.A. Meselhy).

https://doi.org/10.1016/j.otsr.2019.11.033
1877-0568/

Table 1
Demographic data and previous surgeries of the patients included in the study.

No	Age (y)	Gender	Side	A Previous surgery/ies	Time from previous Surgery/ies (y)
1	5	Girl	Lt	1-Plating + graft 2-IM wire + graft 3-Ilizarov bone transport	2.5
2	9	Girl	Rt	1-IM wire + graft 2-Ilizarov bone transport	4
3	3.5	Boy	Lt	IM wire + graft	1
4	4	Girl	Lt	Ilizarov bone transport	1
5	7	Boy	Lt	IM wire + graft	2
6	5	Girl	Rt	Ilizarov bone transport	1
7	8	Boy	Lt	1-IM wire + graft 2- Ilizarov bone transport	4
8	6	Boy	Lt	Ilizarov bone transport	2
9	7	Boy	Lt	1-IM wire + graft 2-Ilizarov bone transport	2.5
10	8	Girl	Rt	IM wire + graft	3
11	6.5	Girl	Lt	IM wire + graft	3.2
12	8.5	Boy	Lt	1-IM wire + graft 2-Ilizarov bone transport	1.6
13	10	Girl	Rt	1-IM wire + graft 2-Ilizarov bone transport	2.1
14	4	Girl	Lt	IM wire + graft	2
15	4.5	boy	Rt	1-IM wire + graft 2-Ilizarov bone transport	3.6
16	5	Girl	Lt	1-IM wire + graft 2-Ilizarov bone transport	1.5
17	6	Boy	Lt	IM wire + graft	3.5
18	5.5	Girl	Lt	IM wire + graft	1.7
19	8	Girl	Rt	1-IM wire + graft 2-Ilizarov bone transport	2

No: number; y: years; Lt: left; Rt: right; IM: intramedullary.

cement (Palacos, Zimmer, Biomet, Warsaw, USA), was placed in the gap. The 2nd stage was performed 4 to 6 weeks later. Cortico-cancellous iliac autograft was obtained from anterior iliac crest and contralateral free non vascularised fibular cortical strut autograft was harvested. The length of the fibular graft was more than the bone defect measured in the 1st stage by 1 to 2 cm. The cement spacer was approached, the membrane was opened carefully along its whole length, the cement was removed, and the proximal and distal bone ends were cleaned from the soft tissue. The strut fibular graft was docked in both tibial ends, and fixed provisionally by trans-plantar K-wire in a retrograde manner with a diameter less than the fibular medullary canal (2 mm in almost all cases). The autogenous iliac graft was then used around the whole length of the fibular strut graft on both medial and lateral borders and around both ends. The membrane was closed carefully around the graft, and the wound was closed. The wire was left in its place until union was achieved.

Patients were followed up every two weeks for the first two months, then monthly till the last follow-up. Every visit, the patients was examined for the stability of the frame and presence of any complications such as pin tract infection and wound complications.

Radiological assessment of callus formation was evaluated according to Hammer et al. [5], After union was achieved clinically and radiographically, the frame and intramedullary K-wire were removed with application of short leg cast for about 12 weeks. Protective leg brace was advised for the next 2 years for all patients. At the last follow-up, measurements were taken to evaluate residual limb deformity and shortening, Malhotra classification of ankle valgus was used to assess ankle deformity [6]; *grade 0* normal fibular physis at the level of plafond, *grade1* the fibular physis at the same level of tibial epiphysis, *grade 2*, at the level of tibial physis, and *grade 3*, fibular physis above that of the tibia.

2.2. Statistical analysis

Statistical comparisons were performed using SPSS (version 13.0; SPSS Inc., Chicago, IL). Clinical data were statistically analyzed using the Mann–Whitney U-test for quantitative data of the term of union time and leg length discrepancy.

3. Results

The 19 patients included 8 boys (42.1%) and 11 girls (57.9%) with mean age of 6.3 years (range: 3.5-10) at time of the first stage. The right side was affected in 6 patients (31.6%) while the left side in 13 patients (68.4%). Ten patients (52.6%) had associated neurofibromatosis type 1 (NF1). Eight patients (42.1%) had associated fibular pseudarthrosis. All patients included in the study were type 4 according to the Crawford classification [7]. The mean previous surgeries before our procedure (Table 1) was 1.5 (range, 1-3). The mean interval from the previous surgeries was 2.3 years (range, 1-4).

The mean interval between the 1st and 2nd stages of the procedure was 4.9 weeks (range, 4–6). The mean bone defect after debridement was 4.5 cm (range, 2.9-6) which represent about 18.98% of the tibial length. The mean length of autogenous fibular graft was 5.54 cm (range, 4.2-7).

The sound bone union was the primary goal, and it was achieved in all patients in a mean time of 25.3 weeks (range: 18.5–32) after the 2nd stage. No significant difference between union time and the number of previous surgical procedures ($p = 0.77$). All patients had a preoperative limb length discrepancy (LLD) with the mean preoperative shortening of 4.9 cm (range, 3.5-5.6). Postoperatively, LLD decreased significantly to 2.96 cm, (range, 1.3-3.8) ($p = 0.001$).

The mean follow-up period was 5.02 years, (range, 2.4-6.5). At final follow-up, all the patients could walk with full weight bearing on the treated limb. None of the patients had permanent protective

Table 2
Union time, fibular graft length, and leg length discrepancy.

No	Time to union (w)	Shortening (cm)		Amount of bone defect	Length of strut fibular graft	Follow up (y)
		Pre	Pop	Cm	Cm	
1	20	4.5	2.2	5.2	7	6.2
2	18.5	5	2	4.9	6.5	5.7
3	23	5.1	3.2	6	6.7	6
4	25	5.5	3.1	4.8	6	4.9
5	32	5.1	3.8	5	7	2.4
6	28	5.5	2.5	4.2	6	4.6
7	22	5.2	3	4.9	5.3	5.2
8	20	5.1	3.1	4.6	5.2	3.5
9	22	5.6	3.1	5	6	5.5
10	25	4.9	1.9	5.3	6	4.7
11	28	5.1	2.7	4.7	5.5	6.2
12	21	5	3.1	4.9	5	6.5
13	30	4.8	1.7	3.7	4.2	5.8
14	32	5	3.2	4.9	5.1	4.7
15	28	4.5	2.2	5	5.2	4
16	27	5.2	2.3	3.5	5	3.5
17	25	4.3	2.1	3.2	5	5.2
18	27	3.5	2.1	2.9	4.2	5.9
19	28	3.6	1.3	3.1	4.5	5

No: number; w: weeks; cm: centimeter; pre: preoperative; pop: postoperative; y: years.

orthosis after the first two years of follow-up. One patient (5.3%) sustained mid-shaft tibial fracture due to fall while playing. This occurred 3 months after brace removal. This patient was treated by above knee cast and sound union was obtained after 12 weeks. Pin tract infection was found in 36.8% of the patients and was treated conservatively with oral antibiotics and local pins care.

There was a valgus ankle deformity in four patients (21%); one patient with grade 1, and three patients with grade 2 (according to Malhotra classification of ankle valgus). This deformity was found in patients with associated fibular pseudarthrosis. The three patients with grade 2 required varus supramalleolar corrective osteotomy to correct the deformity, but patients were satisfied and refused further surgeries. There was no donor site morbidity occurred from iliac graft or fibular graft sites (Table 2).

3.1. Case presentation (patient no. 1)

A 5 years old female patient presented with left congenital pseudarthrosis tibia. The patient underwent multiple operations, the first was plate and graft, second was ipsilateral fibular graft and intramedullary wire, the third was Ilizarov bone transport (Fig. 1). All surgical procedures had failed to achieve the bone union. Shortening was 4.5 cm. Induced membrane technique was performed (Figs. 2 and 3) and union was achieved (Fig. 4) in 20 weeks.

4. Discussion

CPT is a multi-component congenital orthopaedic pathology. Surgical treatment of CPT sometimes fails and repetitive surgeries are quite frequent [8–12]. Pannier et al. [13] concluded that the replacement of fibrous hamartoma and abnormal periosteum by well vascularized biological membrane in association with stable fixation could be an ideal treatment for most of the cases of CPT.

Although the biological explanation of the induced membrane technique in children is still unknown, several hypotheses could be made based on the previous researches in adults [14]. As the induced membrane is highly vascular and contains high concentrations of growth factors. [15], it is used successfully to reconstruct segmental long bone defects in adults [4] and children [16,17].

In the current study, radical excision of the diseased periosteum and the pseudarthrosis was done. The extent of resection was determined intraoperatively by reaching bloody healthy bone on both proximal and distal ends with open medullary canal. Such diseased vascülary impaired periosteum [18] was replaced by the highly vascular induced membrane that helps in achieving union.

Mechanical stability is an essential factor for CPT union. Aurégan and Bégué [19] suggested that the stability of the fixation could be a key to success of the induced membrane technique. Circular frames showed superior results than mono-axial fixators [18,20]. The intramedullary fixation was added to this technique as it provides more mechanical stability by internally splinting the graft [9,10,13]. Finally, the stability could be increased by fibular cortical strut autograft [14,21–24]. In the current study, mechanical stability was provided by Ilizarov circular fixator, intramedullary wire and the non vascularised cortical strut fibular graft that was docked in the medullary canal of proximal and distal tibial ends.

Masquelet et al. [4] recommended the use of strut cortical graft in femur reconstruction to provide stability with morselized iliac autogenous graft. Villemagne et al. [22] and Biau et al. [23] used cortical strut autograft (tibial or fibular) in combination with iliac cancellous autograft. In a trial to solve the problems of limited autograft availability and decrease donor site morbidity, beta-tricalcium phosphate was mixed with the autograft with promising results in adults [25] and children [16]. In the current study, combined non vascularised fibular strut cortical autograft which is longer than the tibial defect and iliac cortico-cancellous chips autograft was used to increase the graft volume which allow for primary stability of the construct and may explain low refracture rate after removal of the fixator.

There were little published researches discussing treatment of CPT after failed multiple surgeries with the treatment option is either vascularized fibular graft or bone transport using Ilizarov external fixator [12,24,26,27]. Table 3 summarise results of some of these studies and showed that our union rate match results obtained by either method. Moreover, induced membrane technique avoids high refracture rates of bone transport and the technical difficulty of vascularized graft.

The strength of this study is the presentation of a homogenous group of patients having CPT after unsuccessful surgeries treated by a relatively new treatment option that achieved excellent results with bone union in all cases. On the other hand, it has several limitations, including a small number of patients, lack of comparison with other treatment modality and lack of long term results.

Fig. 1. Radiographs showing the previous failed operative procedures. A: Plate and screws fixation of the tibia with bone graft. B: Ipsilateral fibular strut graft fixed with intramedullary wire. C: Bone transport by Ilizarovover intramedullary wire.

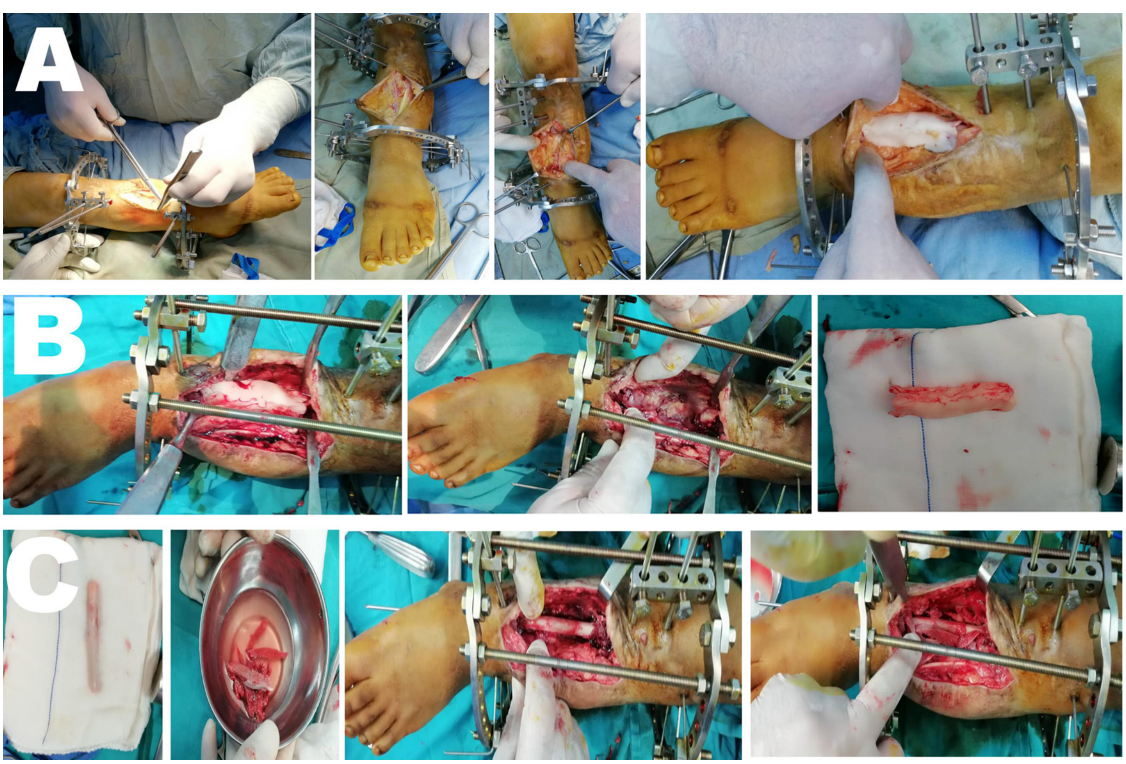

Fig. 2. Clinical pictures showing the induced membrane technique. A: 1st stage: anterolateral approach of the tibia, adequate debridement and cement spacer. B: 2nd stage: the membrane was opened carefully, the cement spacer was removed. C: Cancellous iliac autograft and contralateral free fibular cortical strut autograft wereharvested; the strut fibular graft was fixed with trans-plantar K-wire.

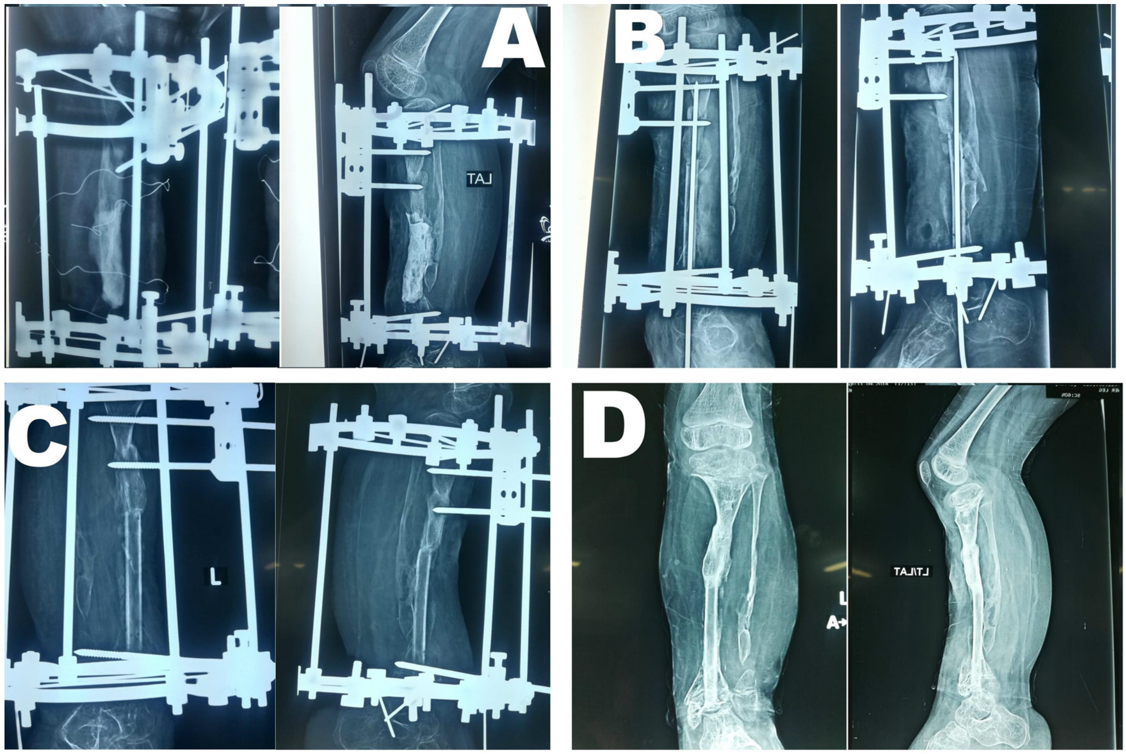

Fig. 3. Radiographs showing the technique. A: 1st stage with cement spacer. B: 2nd stage: cancellous iliac and free fibular strut autografts fixed with K-wire. C: Wire removal to allow ankle motion. D: Anteroposterior and lateral views showing sound union.

Fig. 4. A: Preoperative clinical photos of the left leg showing scars of previous operations and leg deformity. B: Clinical photos after union with the patient fully weight bearing.

Table 3
Summary of similar studies using different techniques.

Study	Yan et al. [12]	Shabtai et al. [23]	Sakamoto et al. [26]	Cho et al. [27]
	2017	2015	2008	2008
Number of patients				
Previous surgery	13	2	5	11
No previous surgery	38	8	3	12
Total	51	10	8	23
Mean age (Years)	3.2	10.5	7	4.7
Neurofiromatosis	45	10	7	19
Fixation	Ilizarov + IM	Ilizarov + IM	Screws	Ilizarov + IM
Graft	Wrapping iliac autograft	Iliac autograft	Vascularized fibular graft	Cortical tibial + iliac cancellous autograft
Mean Follow up	1.6 y	89.1 m	11.7 y	9.2 y
Union	62.7%	100%	100%	100%
Refracture		20%	12%	52%
Pin Tract Infection	11.7%	100%		
Deformity	27.4%	60%	50%	
Limb Shortening	10.6%	50%	23%	

IM: intramedullary; m: months; y: years.

5. Conclusion

The induced membrane technique proved to an effective method in the treatment of unsuccessful previously operated patients of CPT, with high success rate, and relatively few complications.

Ethical approval

The study was approved by the ethical committee of the University (Orth 32-2009) and was in accordance with the ethical standards of the institutional and national research committee.

Consent

Informative consent was obtained from all individual participants included in the study.

Disclosure of interest

The authors declare that they have no competing interest.

Funding

No fund was received.

Authors' contributions

Mohammed Anter Meselhy: study design, surgical performance, data collection, manuscript preparation, editing. Adel Samy Elhammady: data collection, manuscriptpreparation, editing. Mohamed Salah Singer: manuscript preparation and editing.

References

[1] Hatton MJ, Ly T, Noor S, Gollogly JG. Delayed presentation of congenital tibial pseudarthrosis and neurofibromatosis: a difficult union. Asian Biomed 2014;8(1):111–8.
[2] Carney BT, Daniels CL. A retrospective review of congenital pseudarthrosis of the tibia. Iowa Orthop J 2002;22:57–60.
[3] Granchi D, Devescovi V, Baglio SR, et al. Regenerative approach for bone repair in congenital pseudarthrosis of the tibia associated or not associated with type 1 neurofibromatosis: correlation between laboratory findings and clinical outcome. Cytotherapy 2012;14:306–14.
[4] Masquelet AC, Begue T. The concept of induced membrane for reconstruction of long bone defects. Orthop Clin North Am 2010;41:27–37.
[5] Hammer RR, Hammerby S, Lindholm B. Accuracy of radiologic assessment of tibial shaft fracture union in humans. Clin Orthop Relat Res 1985;199:233–8.
[6] Malhotra D, Puri R, Owen R. Valgus deformity of the ankle in children with spina bifida aperta. J Bone Joint Surg 1984;66:381–5.
[7] Crawford AH, Bagamery N. Osseous manifestations of neurofibromatosis in childhood. J Pediatr Orthop 1986;72:88–96.
[8] Grill F, Bollini G, Dungl P, Fixsen J. Treatment approaches for congenital pseudarthrosis of tibia: results of the EPOS multicenter study. European Paediatric Orthopaedic Society (EPOS). J Pediatr Orthop B 2000;75:89–99.
[9] Mathieu L, Vialle R, Thevenin -Lemoineet C. Association of Ilizarov's technique and intramedullary rodding in the treatment of congenital pseudarthrosis of the tibia. J Child Orthop 2008;449:55–62.
[10] Gouron R, Deroussen F, Juvet M. Early resection of congenital pseudarthrosis of the tibia and successful reconstruction using the Masquelet technique. J Bone Joint Surg 2011;552(4):554–93.
[11] Borzunov DY, Chevardin AY, Mitrofanov AI. Management of congenital pseudarthrosis of the tibia with the Ilizarov method in a paediatric population: influence of aetiological factors. Int Orthop 2016;331:339–40.
[12] Yan A, Mei HB, Liu K, Wu JY, Tang J, Zhu GH, et al. Wrapping grafting for congenital pseudarthrosis of the tibia. A preliminary report. Medicine 2017;96:48.
[13] Pannier S, Pejin Z, Dana C, Masquelet AC, Glorion C. Induced membrane technique for the treatment of congenital pseudarthrosis of the tibia: preliminary results of five cases. J Child Orthop 2013;477:485–7.
[14] Aurégan J, Bégué T, Rigoulot G, Glorion C, Pannier S. Success rate and risk factors of failure of the induced membrane technique in children: a systematic review. Injury 2016;47(6 Suppl):S62–7.
[15] Pelissier PH, Masquelet AC, Bareille R. Induced membranes secrete growth factors including vascular and osteoinductive factors and could stimulate bone regeneration. J Orthop Res 2004;22:73–9.
[16] Rousset M, Walle M, Cambou L, Mansour M, Samba A, Pereira B, et al. Chronic infection and infected non-union of the long bones in paediatric patients: preliminary results of bone versus beta-tricalcium phosphate grafting after induced membrane formation. Int Orthop 2018;42(2):385–93.
[17] Gouron R, Deroussen F, Plancq M, Collet L. Bone defect reconstruction in children using the induced membrane technique: a series of 14 cases. Orthop Traumatol Surg Res 2013;99:837–43.
[18] Hermanns-Sachweh B, Senderek J, Alfer J, et al. Vascular changes in the periosteum of congenital pseudarthrosis of the tibia. Pathol Res Pract 2005;305:312–21.
[19] Aurégan JC, Bégué T. Induced membrane for treatment of critical sized bone defect: a review of experimental and clinical experiences. Int Orthop 2014;38:1971–8.
[20] Karger C, Kishi T, Schneider L, Fitoussi F, Masquelet AC, et al. Treatment of posttraumatic bone defects by the induced membrane technique. Orthop Traumatol Surg Res 2012;98(1):97–102.
[21] Masquelet AC, Fitoussi F, Begue T, Muller GP. Reconstruction des os longs par membrane induite et autogreffe spongieuse. Ann Chir Plast Esthet 2000;45:346–53.
[22] Villemagne T, Bonnard C, Accadbled F, L'kaissi M, et al. Intercalary segmental reconstruction of long bones after malignant bone tumor resection using primary methyl methacrylate cement spacer interposition and secondary bone grafting: the induced membrane technique. J Pediatr Orthop 2011;31:570–6.
[23] Biau DJ, Pannier S, Masquelet AC, Glorion C. Case report, reconstruction of a 16-cm diaphyseal defect after Ewing's resection in a child. Clin Orthop 2009;467:572–7.
[24] Shabtai L, Ezra E, Wientroub S, Segev E. Congenital tibial pseudarthrosis, changes in treatment protocol. J Ped Orthop 2015;24(5):444–9.
[25] Sasaki G, Watanabe Y, Miyamoto W, Yasui Y, Morimoto S, Kawano H. Induced membrane technique using beta-tricalcium phosphate for reconstruction of femoral and tibial segmental bone loss due to infection: technical tips and preliminary clinical results. Int Orthop 2018;42(1):17–24.
[26] Sakamoto A, Yoshida T, Uchida Y, Kojima T, Kubota H, Iwamoto Y. Long-term follow-up on the use of vascularized fibular graft for the treatment of congenital pseudarthrosis of the tibia. J Orthop Surg Res 2008;6:3–13.
[27] Cho T-J, Choi IH, Lee SM, et al. Refracture after Ilizarov osteosynthesis in atrophic-type congenital pseudarthrosis of the tibia. J Bone Joint Surg 2008;90–B:488–93.