Rheumatology International (2019) 39:2167–2175
https://doi.org/10.1007/s00296-019-04454-x

Rheumatology
INTERNATIONAL

CASE BASED REVIEW

Platelet-rich plasma for thumb carpometacarpal joint osteoarthritis in a professional pianist: case-based review

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Received: 23 May 2019 / Accepted: 26 September 2019 / Published online: 14 October 2019

Abstract

Thumb carpometacarpal osteoarthritis (TCMC-OA) is a progressively disabling, debilitating condition presenting with thumb base pain and hand functional impairment. Platelet-rich plasma has been used widely for the management of musculoskeletal pathologies, OA being among them. To our knowledge, only a few cases have been previously reported on this topic until now. A 59-year-old male professional pianist presented with chronic, mild onset of right thumb base pain involving a progressive lack of pinch strength in his right hand, and severe difficulties with playing. Three PRP injections were administered to the TCMC joint on a 1-week interval regime. Clinical outcomes were assessed by using the visual analog scale (VAS) for pain, grip and pinch strength, and the Quick-DASH Questionnaire. Functional outcome was excellent according to patient's capability with daily living activities and specific playing demands. At 12 months follow-up, no recurrences or complications were identified, with the musician returning to his previous level of performance 2 weeks before the end of this period. Patient self-reported satisfaction was high and he reported to return to his routine piano activity with no limitations. This case-based review study documents the clinical efficacy of PRP treatment from both functional and perceived-pain perspectives in a professional pianist. Presenting this case, our aim is to draw attention of healthcare providers dealing with TCMC-OA to PRP as a safe, beneficial therapy for this condition which needs further assessment in randomized controlled trials.

Keywords Growth factors · Autologous therapy · Hand injuries · Osteoarthritis · Trapeziometacarpal joint · Thumb

Introduction

Thumb carpometacarpal osteoarthritis (TCMC-OA) is a progressively disabling, debilitating condition presenting with thumb base pain and hand functional impairment that could lead to instability and deformity. Degenerative thumb processes have important functional consequences due to compensatory movements that lead to unbalanced musculoskeletal system during the development of the disease [1], causing pain and decreased mobility which adversely impact patient manipulating capacity, maneuverability, and quality of life [2]. TCMC-OA management has historically involved both conservative and operative approaches according to severity of clinical expression [3]. Conservative

This case report was presented at 11th IFSHT—International Federation of Societies for Hand Therapy and 14th IFSSH—International Federation of Societies for Surgery of the Hand Congress, Berlin 2019 (Abstract no: IFSHT19-1218).

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management includes physiotherapy through joint [4] or nerve [5] mobilization, hand muscles strengthening exercises [6], hand/thumb splinting [1], patient education and activity modification with joint protection regimes [7], oral nonsteroidal anti-inflammatory agents [8], and intra-articular injections. Although these modalities have shown their benefit in the short term, a reasonable doubt exists regarding whether these interventions can alter the natural history or progression of TCMC-OA.

Platelet-rich plasma (PRP) is considered an autologous blood product produced by the centrifugation of whole blood yielding a concentration of platelets above baseline levels [9]. The general rationale for this on OA context lies on the use of a mixture of high concentrations of regenerative proteins that are naturally delivered by thrombocytes, with the purpose to influence and reverse the pro-inflammatory, catabolic environment commonly associated to osteoarthritic disease and consequently restore joint homeostasis [10]. OA has evolved as a specifically benefited target from this technique. OA involves a perturbed joint environment at the cellular level with alterations in the composition of the synovial fluid. The inadequate healing response to synovial inflammation results in further structural cartilage degradation that results on pain and a loss of function [11]. Actually, first scientific reports on PRP use in musculoskeletal conditions included cartilage pathology [12, 13]. Conclusions from experimental studies demonstrated the protective action of PRP and the potential to heal cartilage defects as well as the positive effect on pain and function on hip and knee osteoarthritis [14–18]. However, in spite of its widespread use, conflicting supporting evidence on clinical efficacy of PRP in the management of OA exist. The purpose of this report is to describe the PRP injection regimen strategy used for a professional pianist suffering with a unilateral TCMC-OA who previously failed physical therapy interventions, and to draw attention of healthcare providers to PRP as a useful therapy for this condition.

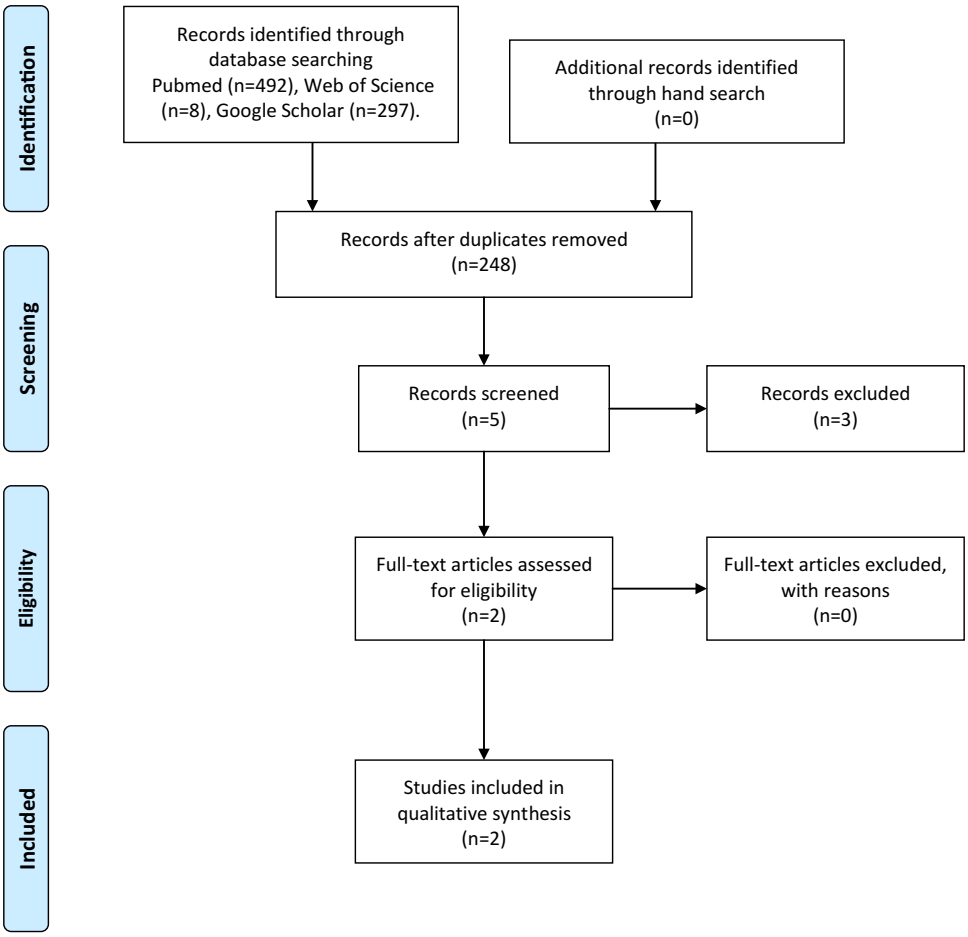

Fig. 1 Hand A-P X-ray view first CMC joint OA

Case presentation

A 59-year-old Caucasian male, right-handed professional pianist suffered from thumb base pain during the last 2 years. He was healthy, pain free until the age of 56, when he first felt impairment of the voluntary movement of his right hand while playing the piano. He thus presented with a 2-year history of insidious, increasing thumb base pain, with progressive lack of pinch strength in his right hand, and severe difficulties with playing. The patient underwent a detailed assessment by an orthopedic surgeon, who discarded surgery. He was referred to our center with a diagnosis of right thumb grade II TCMC-OA, with no instability and minimal dorsal subluxation [19] confirmed by X-ray (Fig. 1) and physical examination. Previous conservative treatments based on conventional physiotherapy—therapeutic ultrasound, manual therapy, activity modifications, and bracing—and acupuncture provided no relief.

On initial examination, patient's right hand revealed a mild CMC joint effusion and palpable lateromedial tenderness with full, active flexion, abduction and extension, and he also experienced pain on pinch resistance on the affected side. No abnormalities in visual and clinical inspection of the other fingers were elicited. The patient's pain worsened with adducting, with a 50% of adduction range-of-motion (ROM) limitation being present, and palpation revealed joint line pain over TCMC. Provocative maneuvers [20] such as grind test, distraction test, and lever test were performed and they elicited a positive result. Thus, he was scheduled for PRP injection 7 days later with informed consent.

Procedure

Forty-five milliliters of whole blood was drawn from patient's antecubital vein using a sterile technique. The procedure originally described by Sanchez et al. was used for the preparation and injection of the platelet concentrate and for the post-injection phase [12, 13]. Blood was collected on 5-mL tubes containing 3.8% (wt/vol) trisodium citrate, then centrifuged at a single spin 447 g (2000 rpm) for 8 min on a certified table-top centrifuge (TMA MEDICA, Nahita, Mod. 2650, Spain) to create upper plasma layer, middle buffy coat layer and a lower red blood cell layer. The lower third plasma fraction located just above the buffy coat was aspirated and dispensed into an empty tube under vertical air-flow conditions.

To receive the treatment, patient sat with the affected hand in a semi-prone position on the table. The intercarpometacarpal space was identified by palpation, the needle tip inserted lateral and medial to the abductor pollicis longus and extensor pollicis brevis tendons. Before each injection, 10% of calcium chloride ($Ca2+ = 0.22$ mEq × dose (ml) was added to the PRP unit to activate platelets shortly before inoculation [21]. After skin sterilization with povidone, PRP was injected into joint through a dorsal [22] and volar [23] approach to the extensor pollicis brevis tendon by using a 25-gauge needle and a 10-ml syringe. Three injections of 3-ml PRP were administered to the TCMC joint with 1-week intervals. Post-injection program consisted of icing locally for 15 min every 1–2 h during the intervention day and the day after, and wearing no brace nor bandage. Heavy activities and sports were discouraged for 48 h after each injection. Adverse events and efficacy were assessed at baseline, 3, and 12 months after the last injection.

Patient follow-up was evaluated using four different, objective outcome measures used to assess patient evolution: visual analog scale (VAS), grip and pinch strength (measured with a Digital Hydraulic Grip/Pinch Gauge, Pro-Med Products, Inc., USA), Kapandji opposition score [24], and the short form of the disabilities of the arm, shoulder, and hand (DASH) questionnaire [25, 26] (QuickDASH, normalized score: 100 indicating the severest disability, and 0 indicating no disability), along with its sports/performing arts module. Satisfaction with the results of the treatment was measured by a 4-point Likert scale. These scores were intended to reflect patient's amelioration through follow-up assessments. Outcomes measures were measured at baseline, 6 weeks and 12 months follow-up.

Supplementary treatments

Patient was instructed not to take nonsteroidal anti-inflammatory drugs during the treatment period in order not to interact with PRP action [27]. Orthosis and physical therapy were also discarded during the treatment period.

Search strategy

Data sources and searches

An electronic database search was performed on PubMed, Scopus, Embase, and Web of Science for cases of TCMC-OA treated with PRP techniques published in English from inception to May 1st, 2019. A combination of the following key terms was used for searching strategy: rhizarthrosis, osteoarthritis, trapeziometacarpal joint, thumb, platelet-rich plasma, and growth factors. Abstracts from relevant studies were reviewed and appropriate articles were retrieved. Manual search was also performed scrutinizing reference lists of the included studies in order to identify additional references [28]. Figure 2 shows the flow diagram depicting the study selection process.

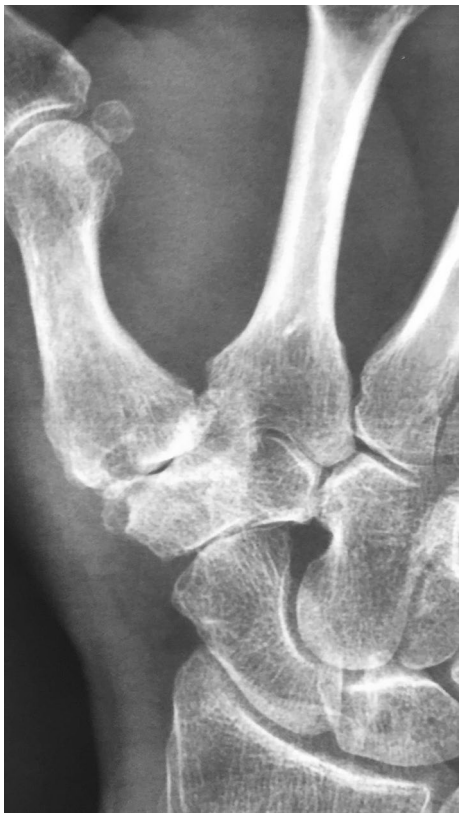

Fig. 2 Flow diagram of the selection process

Study selection

Titles and abstracts were independently scanned by two authors (IM-P, RC-T) based on the following inclusion criteria: (1) cases of TCMC-OA treated with PRP solely; (2) published in English language, and (3) published in a peer-reviewed journal. Grey literature and any study lacking clinical data from individual patients were excluded. No disagreement existed between the two reviewers at any point throughout the selection process.

Data extraction and quality assessment

Two researchers planned to independently extract the following data using a standard form: author, publication year, type of study, sample characteristics, procedure/treatment (number of injections, regimen) intervention arms, measured outcomes, follow-up, and Eaton stage.

Results

No adverse effects were detected and the procedure was well tolerated by the patient. Subject reported only mild joint swelling and discomfort during acute phase post-intervention lasting no longer than a few hours. Significative differences were found during follow-up period when compared to baseline (Table 2). Functional outcome was excellent according to patient's capability with daily living activities and specific playing demands. Patient did not report taking any type of rescue-medication.

At a 6-week follow-up visit, the patient reported a marked reduction of his playing pain and the painful sensation associated to daily living activities disappeared. He was able to play the piano with minimal discomfort at full range. All provocative maneuvers were negative. At 12 months follow-up, no recurrences or complications were identified, with the musician returning to his previous, asymptomatic level of performance 2 weeks before the end of this period. The patient showed excellent recovery with normal and painless thumb movement, total grip (48 kg) and pinch (4.1 kg) strengths, a Kapandji opposition score of 9 (before 6), and a Quick-DASH score of 11 (previously 45). Patient self-reported satisfaction was "4: very satisfied". Generally he was able to use his right hand actively in daily life. He reported to be to his routine piano activity with no limitations, apart from some occasional discomfort in the proximal interphalangeal joint during particular solicitations, such as thumb abduction when playing piano scales during prolonged periods of time.

Only two more research papers have been found in the literature, being a prospective randomized controlled trial (RCT) [29] and a single non-comparative, pilot study [30]. Thus, 26 TCMC-OA cases treated with PRP were identified by this review. Detailed study characteristics are gathered in Table 1. The RCT study included one arm composed by 16 patients who were treated with two PRP injections every 2 weeks, with a significant clinical (VAS) and functional (Quick-DASH) improvement at the short- to mid-term follow-up. Further improvements in both pain and function scores by the end of the first year after treatment were nonsignificant but present [29]. On the other hand, the pilot study reported ten patients who were treated with two TCMC-PRP injections with a 2-week interval, showing significantly lower pain scores and significantly higher Mayo Wrist Scores compared with their pre-treatment values at 6 months follow-up. However, DASH scores remained unaffected [30].

Discussion

TCMC joint of the thumb is the second most frequent site of hand OA following the interphalangeal joints [31, 32]. Both work-related and recreational activities soliciting hand region may play a role in the development of TCMC-OA. Repetitive use of the thumb when performing most daily tasks may contribute to TCMC-OA development [33].

Table 1 Characteristics of included studies

Authors, year	Type of study	Sample size, age (years)	Number of injections, interval	Intervention arms	Measured outcomes	Main results	Follow-up (months)	TCMC-OA Eaton stage in PRP group, number of patients			
								I	II	III	IV
Malahias et al. 2018	RCT	$n=33$, 62.8 ± 10.6	2, 2 wk	PRP group ($n=16$) and steroid+LA group ($n=17$)	Pain (VAS), functional scores (DASH, MWS)	PRP group (12 mo follow-up): VAS decreased 7.5 (5.75–8.00) to 2.0 (1.00–5.25) Q-DASH decreased 50.4 ± 21.6 to 20.4 ± 27.7 and patients' satisfaction rate 69% steroid+LA group (12 mo follow-up): VAS decreased 7.0 (6.00–8.25) to 6.5 (5.0–8.0) Q-DASH decreased 57.9 ± 25.6 to 43.0 ± 27.6 and patients' satisfaction rate 12.5%	Baseline, 3, 6 and 12	NR	NR	NR	NR
Loibl et al. 2016	Pilot study	$n=10$, 56.1 ± 9.9	2, 4 wk	PRP group ($n=10$)	Pain (VAS), DASH, patient's satisfaction	VAS decreased, 6.2 ± 1.6 to 5.4 ± 2.2 (6 mo follow-up) DASH unaffected MWS improved 46.5 ± 18.6 to 67.5 ± 19.0 (6 mo follow-up) grip unaffected pinch declined 6.02 ± 2.99 to 3.96 ± 1.77 (6 mo follow-up)	Baseline, 3, and 6	2	3	5	0

RCT randomized controlled trial, *TCMC-OA* trapeziocarpometacarpal osteoarthritis, *LA* local anesthetic, *VAS* visual analog scale, *DASH* disabilities of the arm, shoulder, and hand, *MWS* Mayo Wrist Score, *wk* weeks, *mo* months

Table 2 Hand and thumb strength scores, functional and pain outcome measures before and after PRP (12 months, follow-up)

	Pre-PRP	Post-PRP 6 wk	Post-PRP 12 m
Quick-DASH[a]	61.36[62.5]	4.54[12.5]	0[0]
VAS (cm)	8	3	1
Grip strength (kg)	31	42	48
Pinch strength (kg)	2.3	3.7	4.1
Kapandji score	6	8	9

Pre-PRP pre-platelet-rich plasma, *Post-PRP* post-platelet-rich plasma, *Quick-DASH* Quick disabilities of the arm, shoulder, and hand [musician module] (range 0–100 [0–100], measures function), *VAS* visual analog scale (range 0–10 cm, measures pain intensity), *wk* weeks, *m* months

[a]Quick-DASH was calculated with sports/performing arts module included

Professional musicians usually spend many hours daily practicing or performing, and they tend to become injured as a result of their crafts [34]. We do present a case clearly related to patient's main activity with no familiar background.

The typical clinical presentation of TCMC-OA includes radial, thumb base pain with an insidious, nontraumatic onset developing over a period of months to years. Deformity, articular rigidity, and ROM limitations usually appear as disease. Actions such as writing and manipulating objects (opening a jar, turning doorknobs) or playing an instrument may be limited and exacerbate symptoms [8]. This patient presented with a grade II TCMC-OA, with no instability and minimal dorsal subluxation. Following three applications of PRP over a period of 2 weeks, we evaluated the efficacy of this treatment using a myriad of validated pain and functional outcome measures (VAS, Quick-DASH, Kapandji score, grip and pinch strength) alongside with a fair follow-up (6 weeks and 12 months). An obvious, significant improvement was identified in all of them, according to the previously reported data, both at mid-term and long-term despite the long-standing structural change and pain chronicity. Patient self-reported satisfaction was accordingly set to be "4: very satisfied".

Management of TCMC-OA has traditionally sought after two major objectives: pain relief and preserved function. The mainstay of treatment remains conservative, nonoperative treatment that focuses on relative rest, orthotic fabrication (splinting), exercises, education in joint protection techniques, and physical modalities (such as heat) are described in the literature for treating TCMC-OA[4,31]. More invasive procedures include hyaluronates and corticosteroid intra-articular injections have been employed, with diverse results. Both European League Against Rheumatism (EULAR) [35] and American College of Rheumatology (ACR) [36] recommendations for the management of hand osteoarthritis stated that there is a paucity of evidence-based data regarding intra-articular injections of long-acting corticosteroid in TCMC-OA. Corticosteroid injections have been proved to provide only temporary relief and may infer harmful effects. Indeed, the corticoid inoculation in this region has been recommended to be carefully considered as it may induce gross cartilage loss and chondrotoxicity at high doses (> 3 mg) [37].

Presently, PRP has been erected as a bridge between conservative modalities and invasive surgical interventions. Growth factors have been demonstrated to play an instrumental role in tissue regeneration and maturation by attracting stem cells and enhancing their differentiation. PRP application indeed has been postulated to reduce the inflammatory process and recreate joint homeostasis within the swelling joint by modifying its biological microenvironment [38]. As soon as PRP is injected into the injured site, platelets are activated by endogenous thrombin and/or intra-articular collagen [39]. After this activation, growth factors such as vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), insulin-like growth factor (IGF), platelet-derived growth factor (PDGF), interleukin-1 receptor antagonist (IL-1RA), soluble receptor of tumor necrosis factor-alpha (TNF-alpha), transforming growth factor-beta (TGF-beta), platelet factor 4 (PF4), as well as osteocalcin, osteonectin, vitronectin, or fibronectin, are secreted by degranulation of the alfa-granules [40, 41]. Globally, these mediators promote an anti-catabolic and anti-inflammatory action in any given condition. IGF, PDGF and TGF-beta play a specific role favoring the stabilization of cartilage by controlling the metabolic functions of chondrocytes and subchondral bone, maintaining synthesis/degradation homeostasis of proteoglycans, promoting chondrocytes proliferation, and decreasing apoptosis [42, 43]. In addition, growth factors have proven to stimulate synovial fibroblasts to synthesize hyaluronic acid [44]. Individually, TGF-beta inhibits cartilage degradation, regulating and enhancing gene expression of tissue inhibitors of metalloproteinases [45, 46]. Therefore, PRP approach may promote a net benefit on OA conditions based on its nature. To our knowledge, only a few cases of TCMC-OA treated by PRP has been documented until now in scientific literature [30].

Although scientific literature involving PRP approach on OA is growing, a comprehensive database search revealed only two studies involving 26 additional cases of TCMC-OA treated with PRP [29, 30]. Clinical and functional outcomes were fair acceptable at mid-term in both cohorts. The case presented herein shows similar results, in spite of dealing with a professional pianist who theoretically assumes higher demanding tasks. In fact, our case might have taken part in any of the referred samples in terms of baseline characteristics (e.g., age, Eaton stage, clinical status) without altering their homogeneity. However, certain differences exist between these two studies and the reported case. First,

regarding the procedure, both total volume injected and number of infiltrations were inferior in these two investigations (Table 1). The PRP administration schedule and dosage in our case included three 3-ml doses at 1-week interval. Second, ultrasound (US) guidance was not used in our case since a small joint was being treated. Conventional palpation-guided anatomical injection has been advocated to result in inaccurate needle placement into extra-articular tissue and adjacent structures. US guidance seems to notably improve injection accuracy in the target intra-articular joint space of large joints [47]. However, certain small joints, particularly the TCMC, diminish the practitioner's accuracy when injecting with the aid of US [48]. Nonetheless, it is well known that both palpation-guided and US procedures are dependent on the user and their experience. According to the reported data, not using US guidance seems not to have represented a limitation in this case.

Among the side effects of PRP, the effects based on the preparation must be distinguished from those based on the administration technique. According to its autologous blood-derived nature, no adverse nor secondary effects are expected when injecting this natural product in any given tissue or region [27]. To date, no compelling evidence of any systemic effect of local PRP administration nor potential cause–effect relationships between growth factors present in PRP and systemic and/or immunogenic diseases have been reported in the literature [27]. Among the adverse effects based on administration technique, there can be certain damage associated to needle penetration, such as haematoma, injury to small blood vessels, pain and sensitivity disorders in the nerve roots, and local/systemic infection due to a nonsterile procedure. However, all these events are extremely rare and can be avoided through compliance with good procedures.

No substantial evidence for the platelet concentration, centrifugation parameters, volume, number of treatments, injection interval (time between injections), location of injection, or PRP composition exist. Our treatment regime was developed on the basis of existing literature regarding PRP approach on OA conditions. Obviously, those protocols treating larger joints involve higher withdrawing of venous blood in order to produce larger amounts of PRP. Thus, further research would contribute to add some light on this topic.

As any other injection procedure, PRP application combine the dry needling stimulus, which tends to induce internal hemorrhage and necessarily an inflammatory response that may lead to a repair process, with the added biological action mediated by injected platelet growth factors. In OA cases this theory has more limitations since this condition preferably expresses intra-articularly. However, it should be taken into consideration.

The use of nonsteroidal anti-inflammatory drugs (NSAIDs) in the early participation period has been postulated to exert an inhibitory effect on healing processes, specially on skeletal muscle [49]. According to its nature, NSAIDs may weaken platelet aggregation and, consequently, PRP actions [50, 51]. However, disagreement exists on the concomitant use of this medication before the PRP treatment or during the first 2 weeks following its application [27]. On the other hand, the inoculation of local anesthesia at the injection site remains controversial [52, 53]. It has been suggested that anesthetic agents may compromise the potential benefit of PRP preparations when coexisting in homeostatic environments by reducing platelets reactivity [54].

Although we are aware that many clinicians may have already included PRP in their treatment algorithms for TCMC-OA, no cases have been reported in the literature. We found that PRP has positive effects in both short term and long-term on TCMC-OA process in terms of hand function and thumb base pain. To the light of these findings, PRP may be considered as a safe, cost-effective, therapeutic procedure in the short- and mid-term follow-up when treating hand OA.

Conclusion

Currently there are limited data regarding PRP approach for TCMC-OA. This case report study documents the clinical efficacy of PRP treatment from both functional and perceived-pain perspectives in a professional pianist, as well as the existing evidence on this topic throughout current scientific literature. Our findings corroborate initial evidence for PRP injections for treatment of pain and impairment associated with TCMC-OA. However, larger controlled, well-designed studies are needed to better guide future PRP treatment guidelines and consolidate it as a safe and effective alternative in TCMC-OA patients.

Acknowledgements The authors would like to gratefully acknowledge the contribution of Raquel Navarro-Ger for her assistance and unconditional encouragement.

Author contributions IM-P conceived, designed and coordinated the study, devised search strategies, drafted the inclusion selection form, wrote and drafted the manuscript; PM-G provided reported data, and analyzed and interpreted the data; SS-DD performed data acquisition, analyzed and interpreted the data, and helped draft the manuscript; MR-E provided critical feedback and helped shape the manuscript; RC-T participated in study design, search strategies, and format advice, and helped revise the manuscript. All authors approved the revised version manuscript and agreed to be accountable for all aspects of the current study.

Funding The authors declared that this study has received no financial support.

Compliance with ethical standards

Conflict of interest Ivan Medina-Porqueres, Pablo Martin-Garcia, Sofia Sanz-De Diego, Marcelo Reyes-Eldblom, and Raquel Cantero-Tellez declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. All authors fulfilled the ICMJE authorship criteria.

Informed consent Written informed consent was obtained from the patient prior to submission of this article for consideration as a case-based review.

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