Bone 121 (2019) 68–71

Contents lists available at ScienceDirect

Bone

journal homepage: www.elsevier.com/locate/bone

Full Length Article

Serum periostin levels and severity of fibrous dysplasia of bone

H. Guerin Lemaire[a,*], B. Merle[b], O. Borel[b], D. Gensburger[b], R. Chapurlat[b]

[a] Department of Rheumatology, Edouard Herriot University Hospital, 5 Place d'Arsonval, 69003 Lyon, France
[b] INSERM UMR 1033, Université de Lyon, Division of Rheumatology, Edouard Herriot University Hospital, 5 Place d'Arsonval, 69003 Lyon, France

ARTICLE INFO

Keywords:
Fibrous dysplasia of the bone
Periostin
Bisphosphonates
McCune-Albright syndrome

ABSTRACT

Fibrous dysplasia of bone (FD) is a rare congenital bone disease, characterized by a fibrous component in the bone marrow. Periostin has been extensively researched because of its implication in various fibrotic or inflammatory diseases. Periostin may be associated with the burden or the severity of FD.

The case control PERIOSDYS study aimed at assessing serum periostin levels in FD patients. Sixty four patients with monostotic or polyostotic disease were included, in order to evaluate whether the concentrations were greater in patients than in 128 healthy age, BMI and sex-matched controls and if they were more elevated in patients with the more severe phenotypes.

We found that periostin levels were greater in patients with FD compared to controls (mean = 1085 vs 958 pmol/l, p = 0.026), especially in those with a history of fracture (mean = 1475 vs 966 pmol/l, p = 0.0005), polyostotic forms (mean = 1214 vs 955 pmol/l, p = 0.004) or McCune-Albright syndrome (mean = 1585 vs 1023 pmol/l, p = 0.0048). In contrast, high pain levels were not associated with periostin levels (mean = 1137 vs 1036 pmol/l, p = 0.445). Furthermore, patients undergoing bisphosphonate therapy had significantly lower levels than treatment naïve patients (mean = 953 vs 1370 pmol/l, p = 0.002).

In conclusion, periostin may be a biochemical marker indicative of the most severe forms of FD and could be used to monitor patients treated with bisphosphonates.

1. Introduction

Fibrous dysplasia of bone (FD) is a rare bone disease, congenital but not hereditary, due to a somatic mutation of GNAS [1]. Its histologic hallmark is the replacement of normal bone by a proliferation of fibrous connective tissue with woven bone trabeculae [2]. The clinical presentation of FD is extremely variable among patients: some will have a mild if not asymptomatic form, whereas some will present with severe impairment [3]. FD may either occur as an isolated condition or as part of the McCune-Albright syndrome (MAS), which is characterized by the following triad: FD, hyperfunctioning endocrinopathies (mainly peripheral precocious puberty), and/or café-au-lait spots. A sizeable number of patients have renal phosphate wasting because mutated cells produce excess amounts of the phosphate-regulating hormone fibroblast growth factor-23 (FGF23), leading to loss of phosphate in the urine.

To date, it has been challenging to determine the prognosis of a given patient. We know that patients with the highest burden of disease - e.g., those with polyostotic disease - have more fractures [4], as this is also the case for those with renal phosphate wasting [5]. Nevertheless, there is no specific serum marker for FD, and the existing biochemical markers of bone turnover show little correlation with the prognosis [6]. A scintigraphic skeletal burden score has been developed, able to predict functional outcome [7]. This score is essentially based on the initial spread of the disease, but does not account for the intrinsic biological activity of some bone lesions. In addition, the occurrence of bone pain has been considered largely unrelated to the disease burden [4].

Given the broad clinical spectrum of the condition, developing simple markers of disease severity is warranted. Periostin is an extra cellular matrix protein [8]. It has been shown to be involved in a variety of conditions where dysregulated inflammation leads to the development of fibrosis, partly mediated by this protein [9]. Furthermore, it is known to be overexpressed in the cells of patients with FD, and it is found in the pathologic fibrous component of the bone of patients with FD [10]. Periostin has also been associated with bone fragility in a cohort of healthy postmenopausal women [11] and the progression of knee osteoarthritis [12]. So, periostin may be of interest in exploring the bone consequences of FD. Therefore, we sought to determine whether serum periostin was associated with the severity of FD. We conducted a case-control study, the PERIOSDYS study, in order to assess the relationship of serum periostin with the characteristics of the disease in patients with FD.

* Corresponding author.
E-mail address: Helene.lemaire@chu-lyon.fr (H. Guerin Lemaire).

https://doi.org/10.1016/j.bone.2019.01.004
Received 28 August 2018; Received in revised form 4 December 2018; Accepted 3 January 2019
Available online 04 January 2019
8756-3282/

2. Material and methods

2.1. Study design and participants

In this case-control, monocentric study, conducted at a national reference center for FD (the Edouard Herriot University Hospital in Lyon, France), we have recruited 64 patients between May 2016 and May 2018. Eligible participants were adults over the age of 18, diagnosed with FD and able to understand and sign the consent forms. The main exclusion criteria were pregnancy and history of another condition known to increase serum periostin levels (such as severe allergic asthma, metastatic cancer, or scleroderma). The recruitment was conducted either during a hospitalization or during a simple consultation. Controls were drawn from preexisting population-based cohorts of healthy patients currently on follow-up in our research group: the OFELY [13], MODAM [14] and STRAMBO [15] cohorts.

The PERIOSDYS study was sponsored by Hospices Civils de Lyon and received IRB approval (CPP n°15/075, April 5th, 2016).

2.2. Measurements

Patients were included after signing informed consent forms. Two blood samples were taken for each patient and then frozen for later analysis of the serum. We used a sandwich ELISA (enzyme-linked immunosorbent assay) which can measure equally every known isoform of periostin (Biomedica, Vienna, Austria). The intra assay coefficient of variation is inferior to 3%, and the inter assay inferior to 6% with this kit. Results are expressed in pmol/l. Sub groups of patients were also formed using: form of the disease (polyostotic vs monostotic), pain > 3 using the numerical pain scale (in which the patient selects a whole number between 0 and 10 that best reflects the intensity of his pain), history of fracture, previous treatment with bisphosphonate, associated McCune-Albright syndrome. FGF23 levels were also collected when available.

2.3. Outcome measures

The primary endpoint was the concentration of serum periostin in FD patients and healthy controls, to examine the association between this marker and the disease. The secondary endpoints were the concentrations of periostin in the various forms of the disease (mono versus polyostotic), fractured vs non fractured, painful vs non painful and in the presence of an associated MAS.

2.4. Statistical analysis

Serum periostin level for each patient was compared to that of two healthy controls, matched for age, sex and BMI. We used a student *t*-test to test the significance of differences in mean concentrations of periostin. We then carried out a linear regression analysis in order to assess the relationship between serum periostin, MAS, prior treatment with bisphosphonates and age. Then a multivariate analysis was performed to insure that each previous variable was independently associated with an increased concentration. All analyses were performed using STATA 12.

3. Results

We enrolled 64 patients with FD, 69% women and 31% men, including 7 patients with MAS, 2 with Mazabraud syndrome and 3 with renal phosphate wasting. The mean age was 44.5. Half of the patients presented with a monostotic form of the disease, the other half with a polyostotic form. Twenty four percent of patients had prevalent fracture, but only three had fractured during the previous year, and 68% were on IV bisphosphonate therapy (Table 1). The majority of patients (91%) were treated with pamidronate, and only 9% were treated with zoledronic acid. Patients in the treated group were either currently under treatment or had received bisphosphonate therapy in the previous year. Patients in the untreated group were either treatment naïve or had not received bisphosphonate for at least five years. Among polyostotic patients, 12 had a history of fracture (37%) and 53% were undergoing bisphosphonate therapy. Among fractured patients, 75% had a polyostotic form. Among the treated patients, 8 had a history of fracture (18%) and 18 (40%) had a polyostotic form.

Table 1
Patients characteristics.

	Controls	Patients
Number	128	64
Age, mean (year)	42.9	44.5
BMI, mean	27.3	28.1
Women, n (%)	88 (69%)	44 (69%)
Form, n (%)		
Polyostotic		32 (50%)
Monostotic		32 (50%)
Bisphosphonate therapy, n (%)		44 (68%)
Prevalent fracture, n (%)		16 (24%)
McCune-Albright, n		7
Phosphate wasting, n		3
Mazabraud, n		2
Bone pain (VAS > 3), n (%)		28 (44%)

Periostin concentrations were significantly greater in FD patients than in controls (1085.2 pmol/l vs 9584, p = 0.026), as shown in Fig. 1. Among patients, periostin levels were significantly more elevated in patients with previous fracture (1475 pmol/l vs 966, p = 0.0005, n = 64), as shown in Fig. 2. Most of these fractures were not recent (only 3 had occurred in the year before the periostin measurement). Periostin was also increased in those with a polyostotic form (1214 pmol/l vs 955.7, p = 0.004) as shown in Fig. 3, and in those with MAS (1585.1 pmol/l vs 1023.8, p = 0.0048). Periostin was not significantly increased in patients presenting with pain > 3 using the numerical pain scale, as well as in patients presenting with clinically more severe forms of FD, defined by a composite endpoint comprising pain, polyostotic form and fracture. Periostin levels were significantly lower in patient receiving bisphosphonate therapy (953.6 pmol/l vs 1370.7, p = 0.002).

The regression analysis showed that history of fracture (p = 0.0005), ongoing bisphosphonate therapy (p = 0.0020), MAS (p = 0.0048) and polyostotic form (p = 0.040) were significantly

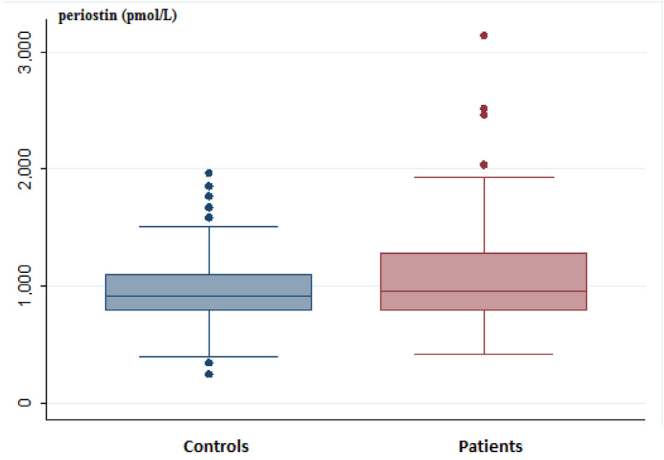

Fig. 1. Serum periostin in controls (blue box, n = 128) and in patients (red box, n = 64) showing that periostin concentrations were significantly greater in FD patients than in controls (p = 0.026). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

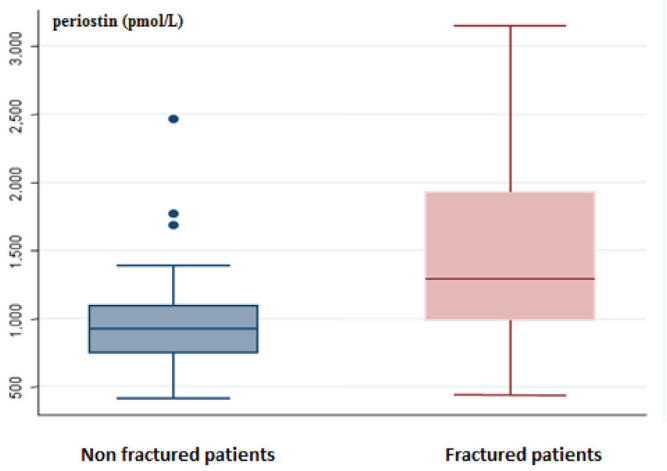

Fig. 2. Serum periostin in non-fractured (blue box, n = 48) and fractured patients (red box, n = 16) showing that the concentrations were significantly greater in fractured patients than in non-fractured patients (p = 0.0005). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

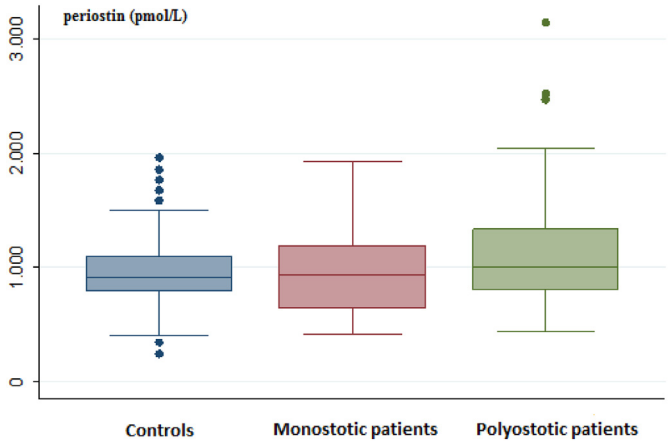

Fig. 3. Serum periostin in controls (blue box, n = 128), monostotic patients (red box, n = 32) and polyostotic patients (green box, n = 32) showing that the concentrations were significantly greater in polyostotic patients than in controls (p = 0.004). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

associated with serum periostin level, whereas age was not (p = 0.98).

The multivariate analysis showed that a history of fracture was independently associated with a greater concentration after adjustment for the form of the disease, and the association with MAS (p = 0.015).

Furthermore, CTX levels were correlated to periostin levels with a Pearson correlation coefficient r = 0.4561 (p = 0.004). But this association was found neither in the subgroup of treated patients (p = 0.119) nor in the subgroup of treated patients (p = 0.18). FGF23 levels were available for only 33 patients. There was no correlation between periostin and FGF23 levels with a Pearson correlation coefficient r = 0.071 (p = 0.69).

Lastly, periostin levels were also strongly correlated to the number of bone lesions in patients (r = 0.599, p < 0.001).

4. Discussion

We found that serum periostin was increased in FD patients compared with healthy controls, especially those with the most severe forms, including a polyostotic disease and prevalent fracture. There was no association with bone pain.

In healthy individuals, periostin has been shown to be physiologically involved in tissue reparation after an injury (e.g., myocardial infarction and fracture [9]) and in fibrotic or inflammatory diseases, such as scleroderma or severe allergic asthma [16] [17]. An inappropriate tissue remodeling occurs through a sustained upregulation of periostin in response to a recurring stimulus, leading to fibrosis. No studies were conducted in FD patients so far, even though it has been proven to be involved in the cellular pathways leading to the disease [10]. In the case of FD, the genetic abnormality itself is responsible for the increased production of periostin by the mutated osteoblasts.

Serum periostin was greater in patients with a history of fracture. Now a prospective study would be warranted to prove that periostin could be a predictive marker of the risk of fracture in those with FD. Of note, periostin has already been shown to be associated with the risk of fragility fracture in postmenopausal women [11] but in our younger patients the mechanism is likely to be different and linked to the pathophysiology of FD. Periostin may ultimately have a negative impact on bone strength and fracture repair. Our result is unlikely to be influenced by recent fractures, which were a small minority (n = 3). In those three cases, it is then difficult to assess whether the high levels were due to the disease or the fracture, since periostin is known to be increased after a fracture [18].

Interestingly, our study also shows that periostin levels are significantly lower in patients undergoing bisphosphonate therapy. Of note, one study in mice and another one in post-menopausal women showed that periostin levels were not affected by these therapies [19] [20]. In addition, periostin has been shown to be degraded by cathepsin K during the bone resorption process [21]. So, one could expect that periostin is not decreased in patients with FD on bisphosphonates. The decrease we observed suggests that bisphosphonates might have an effect on the pathophysiology of the disease. It was previously suspected that bisphosphonates were effective in the treatment of FD through their antiresorptive action, as mutated osteoblasts produce IL-6 and RANKL which activate osteoclasts [22]; but this pathway does not involve periostin, and therefore does not explain the lower levels observed in treated patients. Compounds that increase bone formation - such as parathyroid hormone and teriparatide - increase serum periostin [23], but these drugs are contraindicated in FD owing to the increased risk of sarcoma.

Moreover, increased periostin is also associated with tumor progression, poorer prognosis and a trend to increased incidence of metastasis in a large variety of cancers. It is believed to play a role during invasion, angiogenesis, and metastasis [9]. More specifically, it has been proven to be an independent prognostic factor in osteosarcoma patients, correlated to poor survival [24]. Likewise, one study showed that periostin is elevated in the serum and bone marrow plasma of patients with myeloma and correlates with advanced disease features, pathological fractures, diffuse MRI pattern of marrow infiltration and LDH at diagnosis [25]. Furthermore, it is increased in patients with bone metastasis, especially in breast cancer, with poor clinical outcome [26] [27]. All of the above support the influence of elevated periostin in the progression of the tumor, and more broadly in the disease activity. It may have the same consequences on FD lesions, which to some extent might behave as bone tumors.

There was no significant correlation between pain and periostin levels. It is nevertheless a major concern for FD patients, as up to 81% of adult patients report suffering from pain [28], which can sometimes be intense and severely hamper the patients quality of life. To date, pathophysiology of pain in FD remains unclear. It was shown to have a tendency to increase with time, and not to be correlated to the skeletal burden of the disease [28]. It has been suggested that bone remodeling is not the only cause, but that modification of nerve fibers that innervate the bone may be involved as well [29], which may explain the lack of correlation between bone markers and pain evaluation. Other leads have to be explored to have a better understanding of pain mechanisms in FD.

Lastly, we found a correlation between periostin and CTX levels. This association, however, was found neither in the subgroup of treated patients nor in the subgroup of non-treated patients, probably due to a lack of statistical power. There was no correlation between periostin and FGF-23 serum levels. FGF-23 is a circulating factor, mainly synthesized by osteocytes, that negatively regulates serum levels of inorganic phosphorous and 1,25(OH)2D3, and is not captured within bone [30]. Its production by the abnormal osteogenic precursors is increased in FD, and it has also been shown that its processing is modified, with increased proteolysis and increased circulating inactive forms [31]. While significant hypophosphatemia is rare and correlated with disease severity and tissue burden [32], minimal phosphate wasting is quite common. In that regard, one could have expected to find a correlation to periostin levels, both being produced by the mutated cells and linked to disease severity. The small number of patients might be a reason why we were unable to show such correlation.

The limitations of this study were the small number of patients, and the fact that this case control study did not allow us to carry out a kinetic analysis of the periostin concentrations, which would be warranted to get a better understanding of the responsibility of periostin in fractures, and on a possible role of bisphosphonates on the intrinsic activity of the lesions. Lastly, the assay used in this study measured all isotypes of periostin. Given the new data on the degradation of periostin by cathepsin K during bone resorption and the broad expression of periostin in various tissue and diseases, it would be interesting to use an assay with a better specificity for periostin originating from bone.

5. Conclusion

In conclusion, serum periostin levels were significantly greater in patients with FD compared with healthy controls, particularly in patients with history of fracture, polyostotic forms and MAS. Interestingly, patients undergoing bisphosphonate therapy had significantly lower levels than treatment naïve patients. Prospective studies will determine whether periostin could become a prognostic marker of FD and whether it can be used as a monitoring tool.

Funding

This work was supported by INSERM, France.

Role of the funding source

The study was conducted thanks to intramural funding from INSERM, that had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and takes final responsibility for the decision to submit for publication.

References

[1] L.S. Weinstein, G(s)alpha mutations in fibrous dysplasia and McCune-Albright syndrome, J. Bone Miner. Res. Off. J. Am. Soc. Bone Miner. Res. 21 (Suppl. 2) (déc 2006) P120–P124.
[2] M. Riminucci, B. Liu, A. Corsi, A. Shenker, A.M. Spiegel, P.G. Robey, et al., The histopathology of fibrous dysplasia of bone in patients with activating mutations of the Gs alpha gene: site-specific patterns and recurrent histological hallmarks, J. Pathol. 187 (2) (janv 1999) 249–258.
[3] R.D. Chapurlat, P. Orcel, Fibrous dysplasia of bone and McCune–Albright syndrome, Best Pract. Res. Clin. Rheumatol. 22 (1) (mars 2008) 55–69.
[4] J. Benhamou, D. Gensburger, C. Messiaen, R. Chapurlat, Prognostic factors from an epidemiologic evaluation of fibrous dysplasia of bone in a modern cohort: the FRANCEDYS study, J. Bone Miner. Res. Off. J. Am. Soc. Bone Miner. Res. 31 (12) (déc 2016) 2167–2172.
[5] A.I. Leet, C. Chebli, H. Kushner, C.C. Chen, M.H. Kelly, B.A. Brillante, et al., Fracture incidence in polyostotic fibrous dysplasia and the McCune-Albright syndrome, J. Bone Miner. Res. Off. J. Am. Soc. Bone Miner. Res. 19 (4) (avr 2004) 571–577.
[6] R.D. Chapurlat, P. Hugueny, P.D. Delmas, P.J. Meunier, Treatment of fibrous dysplasia of bone with intravenous pamidronate: long-term effectiveness and evaluation of predictors of response to treatment, Bone 35 (1) (juill 2004) 235–242.
[7] M.T. Collins, H. Kushner, J.C. Reynolds, C. Chebli, M.H. Kelly, A. Gupta, et al., An instrument to measure skeletal burden and predict functional outcome in fibrous dysplasia of bone, J. Bone Miner. Res. Off. J. Am. Soc. Bone Miner. Res. 20 (2) (févr 2005) 219–226.
[8] N. Bonnet, P. Garnero, S. Ferrari, Periostin action in bone, Mol. Cell. Endocrinol. 432 (2016) 75–82 (05).
[9] S.J. Conway, K. Izuhara, Y. Kudo, J. Litvin, R. Markwald, G. Ouyang, et al., The role of periostin in tissue remodeling across health and disease, Cell. Mol. Life Sci. 71 (7) (avr 2014) 1279–1288.
[10] T.G. Kashima, T. Nishiyama, K. Shimazu, M. Shimazaki, I. Kii, A.E. Grigoriadis, et al., Periostin, a novel marker of intramembranous ossification, is expressed in fibrous dysplasia and in c-Fos-overexpressing bone lesions, Hum. Pathol. 40 (2) (févr 2009) 226–237.
[11] J.C. Rousseau, E. Sornay-Rendu, C. Bertholon, R. Chapurlat, P. Garnero, Serum periostin is associated with fracture risk in postmenopausal women: a 7-year prospective analysis of the OFELY study, J. Clin. Endocrinol. Metab. 99 (7) (juill 2014) 2533–2539.
[12] J.C. Rousseau, E. Sornay-Rendu, C. Bertholon, P. Garnero, R. Chapurlat, Serum periostin is associated with prevalent knee osteoarthritis and disease incidence/progression in women: the OFELY study, Osteoarthr. Cartil. 23 (10) (oct 2015) 1736–1742.
[13] E. Sornay-Rendu, S. Boutroy, F. Duboeuf, R.D. Chapurlat, Bone microarchitecture assessed by HR-pQCT as predictor of fracture risk in postmenopausal women: the OFELY study, J. Bone Miner. Res. Off. J. Am. Soc. Bone Miner. Res. 32 (6) (juin 2017) 1243–1251.
[14] H. Nagy, R. Chapurlat, E. Sornay-Rendu, S. Boutroy, P. Szulc, Family resemblance of bone turnover rate in mothers and daughters—the MODAM study, Osteoporos. Int. 26 (3) (mars 2015) 921–930.
[15] P. Szulc, S. Boutroy, R. Chapurlat, Prediction of fractures in men using bone microarchitectural parameters assessed by high-resolution peripheral quantitative computed tomography-the prospective STRAMBO study, J. Bone Miner. Res. Off. J. Am. Soc. Bone Miner. Res. 33 (8) (25 avr 2018) 1470–1479.
[16] Y. Yamaguchi, J. Ono, M. Masuoka, S. Ohta, K. Izuhara, Z. Ikezawa, et al., Serum periostin levels are correlated with progressive skin sclerosis in patients with systemic sclerosis, Br. J. Dermatol. 168 (4) (1 avr 2013) 717–725.
[17] L.B. Richards, A.H. Neerincx, van Bragt JJMH, P.J. Sterk, E.H.D. Bel, A.H. Maitland-van der Zee, Biomarkers and asthma management: analysis and potential applications, Curr. Opin. Allergy Clin. Immunol. 18 (2) (avr 2018) 96–108.
[18] J. Yan, H.J. Liu, H. Li, L. Chen, Y.Q. Bian, B. Zhao, et al., Circulating periostin levels increase in association with bone density loss and healing progression during the early phase of hip fracture in Chinese older women, Osteoporos. Int. 28 (8) (août 2017) 2335–2341.
[19] S. Contié, N. Voorzanger-Rousselot, J. Litvin, N. Bonnet, S. Ferrari, P. Clézardin, et al., Development of a new ELISA for serum periostin: evaluation of growth-related changes and bisphosphonate treatment in mice, Calcif. Tissue Int. 87 (4) (oct 2010) 341–350.
[20] A.D. Anastasilakis, S.A. Polyzos, P. Makras, M. Savvides, G.T. Sakellariou, A. Gkiomisi, et al., Circulating periostin levels do not differ between postmenopausal women with normal and low bone mass and are not affected by zoledronic acid treatment, Horm. Metab. Res. 46 (2) (févr 2014) 145–149.
[21] N. Bonnet, J. Brun, J.-C. Rousseau, L.T. Duong, S.L. Ferrari, Cathepsin K controls cortical bone formation by degrading periostin, J. Bone Miner. Res. Off. J. Am. Soc. Bone Miner. Res. 32 (7) (juill 2017) 1432–1441.
[22] S.A. Kuznetsov, N. Cherman, M. Riminucci, M.T. Collins, P.G. Robey, P. Bianco, Age-dependent demise of GNAS-mutated skeletal stem cells and “normalization” of fibrous dysplasia of bone, J. Bone Miner. Res. Off. J. Am. Soc. Bone Miner. Res. 23 (11) (nov 2008) 1731–1740.
[23] F. Gossiel, J.R. Scott, M.A. Paggiosi, K.E. Naylor, E.V. McCloskey, N.F.A. Peel, et al., The effect of teriparatide treatment on circulating periostin and its relationship to regulators of bone formation and BMD in postmenopausal women with osteoporosis, J. Clin. Endocrinol. Metab. 103 (4) (22 janv 2018) 1302–1409.
[24] F. Hu, X.-F. Shang, W. Wang, W. Jiang, C. Fang, D. Tan, et al., High-level expression of periostin is significantly correlated with tumour angiogenesis and poor prognosis in osteosarcoma, Int. J. Exp. Pathol. 97 (1) (févr 2016) 86–92.
[25] E. Terpos, D. Christoulas, E. Kastritis, T. Bagratuni, M. Gavriatopoulou, M. Roussou, et al., High levels of periostin correlate with increased fracture rate, diffuse MRI pattern, abnormal bone remodeling and advanced disease stage in patients with newly diagnosed symptomatic multiple myeloma, Blood Cancer J. 6 (10) (2016) e482 (07).
[26] D. Xu, H. Xu, Y. Ren, C. Liu, X. Wang, H. Zhang, et al., Cancer stem cell-related gene periostin: a novel prognostic marker for breast cancer, PLoS One 7 (10) (2012) e46670.
[27] E. Gineyts, N. Bonnet, C. Bertholon, M. Millet, A. Pagnon-Minot, O. Borel, et al., The C-terminal intact forms of periostin (iPTN) are surrogate markers for osteolytic lesions in experimental breast cancer bone metastasis, Calcif. Tissue Int. 105 (5) (18 juin 2018) 567–580.
[28] M.H. Kelly, B. Brillante, M.T. Collins, Pain in fibrous dysplasia of bone: age-related changes and the anatomical distribution of skeletal lesions, Osteoporos. Int. 19 (1) (janv 2008) 57–63.
[29] R.D. Chapurlat, D. Gensburger, J.M. Jimenez-Andrade, J.R. Ghilardi, M. Kelly, P. Mantyh, Pathophysiology and medical treatment of pain in fibrous dysplasia of bone, Orphanet. J. Rare Dis. 7 (Suppl. 1) (24 mai 2012) S3.
[30] R.D. Chapurlat, C.B. Confavreux, Novel biological markers of bone: from bone metabolism to bone physiology, Rheumatology 55 (10) (1 oct 2016) 1714–1725.
[31] N. Bhattacharyya, M. Wiench, C. Dumitrescu, B.M. Connolly, T.H. Bugge, H.V. Patel, et al., Mechanism of FGF23 processing in fibrous dysplasia, J. Bone Miner. Res. Off. J. Am. Soc. Bone Miner. Res. 27 (5) (mai 2012) 1132–1141.
[32] M. Riminucci, M.T. Collins, N.S. Fedarko, N. Cherman, A. Corsi, K.E. White, et al., FGF-23 in fibrous dysplasia of bone and its relationship to renal phosphate wasting, J. Clin. Invest. 112 (5) (sept 2003) 683–692.