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Teaching cases

Multiple metachronus proliferative fasciitis occurring in different anatomic regions: A case report and review of the literature

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ABSTRACT

Proliferative fasciitis is a benign lesion that usually has a self-limited course and rarely recurs after excision. In the literature, the multifocal occurrence of PF in different anatomic sites has not been reported so far.

In this report, we describe the clinical case of a 30-year-old woman with two metachronous proliferative fasciitis occurring firstly in the orbit and, after 18 months, in the forearm; we also review the available literature on this topic, outlining guidelines for therapy and the follow-up of these patients.

Introduction

Proliferative fasciitis (PF) is a pseudo-sarcomatous lesion typically involving the subcutaneous tissue and fascia. It belongs to a heterogeneous group of reactive soft tissue proliferative lesions, such as nodular fasciitis and proliferative myositis. PF develops more frequently in the upper extremities, particularly the forearms, followed by the lower extremities and the trunk. It tends to grow rapidly and to clinically simulate a malignant mesenchymal tumor [1–4]. Local recurrence of PF is extremely rare. In the literature, the concurrent or metachronous occurrence of multiple PF in different anatomic regions has not been reported so far, and there are a few data on the treatment and follow up modalities of these patients. In this study, we report the case of a young woman with recurrent PF. Indeed, in this patient, a primary diagnosis of PF involving the left orbital region was made, and, after more than one year, the occurrence of a similar lesion in a distant anatomical site was found. A review of the current literature, focusing on histological diagnosis and clinical outcome, is also reported.

Case report

On January 2008, a 30-year-old woman came to our attention with a left orbital mass, first noticed a month earlier, when she woke up with left eye puffiness, difficulties opening the left eyelid, and diplopy. The patient was otherwise healthy and reported no previous trauma at the site of the lesion. At the physical examination, the left orbital mass was associated with exophthalmos and tenderness at both superficial and deep palpation. However, the pupils were round, equal, reactive to light with direct and consensual response, and normally able to accommodate; the ocular motility was orthotropic with normal visual acuity. MRI imaging of the lesion showed, at the upper quadrants of the left eye-socket, a 1.5 cm mass compressing and caudally dislocating the superior rectus muscle and the left eyeball (Fig. 1a). The left optic nerve was smaller than the right one and was caudally dislocated. The lesion was excised with an orbitotomy under local anesthesia. The nodule was 10 mm large, white-grayish, fibrous in aspect, and irregular in shape. Histologically, it was composed of variably cellular areas containing medium- to large-sized spindle, stellate, and ganglion-like cells with abundant cytoplasm and vesicular nuclei with prominent nucleoli. These cells were variably embedded in a fibrous to myxoid stroma. Ganglion-like cells were both mono- or bi-nucleated cells (Fig. 1b and c). Spindled cells showed nuclei with compact chromatin and inconspicuous nucleoli, if any, without cytological atypia. There were 1–2 normal mitotic figures per 10/HPF, and atypical mitoses were not present. Vascular structures, erythrocyte extravasation, and an inflammatory component represented by lymphocytes were also present. Conventional immunostain was performed on additional sections using a Ventana Benchmark (Ventana Tuxon AZ) using the following prediluted monoclonal antibodies SMA (smooth muscle actin), Desmin, Vimentin, Myogenin, S100, Ki67, Bcl-2, and CD34 (Ventana Tuxon AZ). The immunohistochemical profile was positive for Vimentin and SMA (Fig. 1d), presented a low Ki-67 labeling index, was negative for CD34, bcl-2, S100, myogenin, and showed focal

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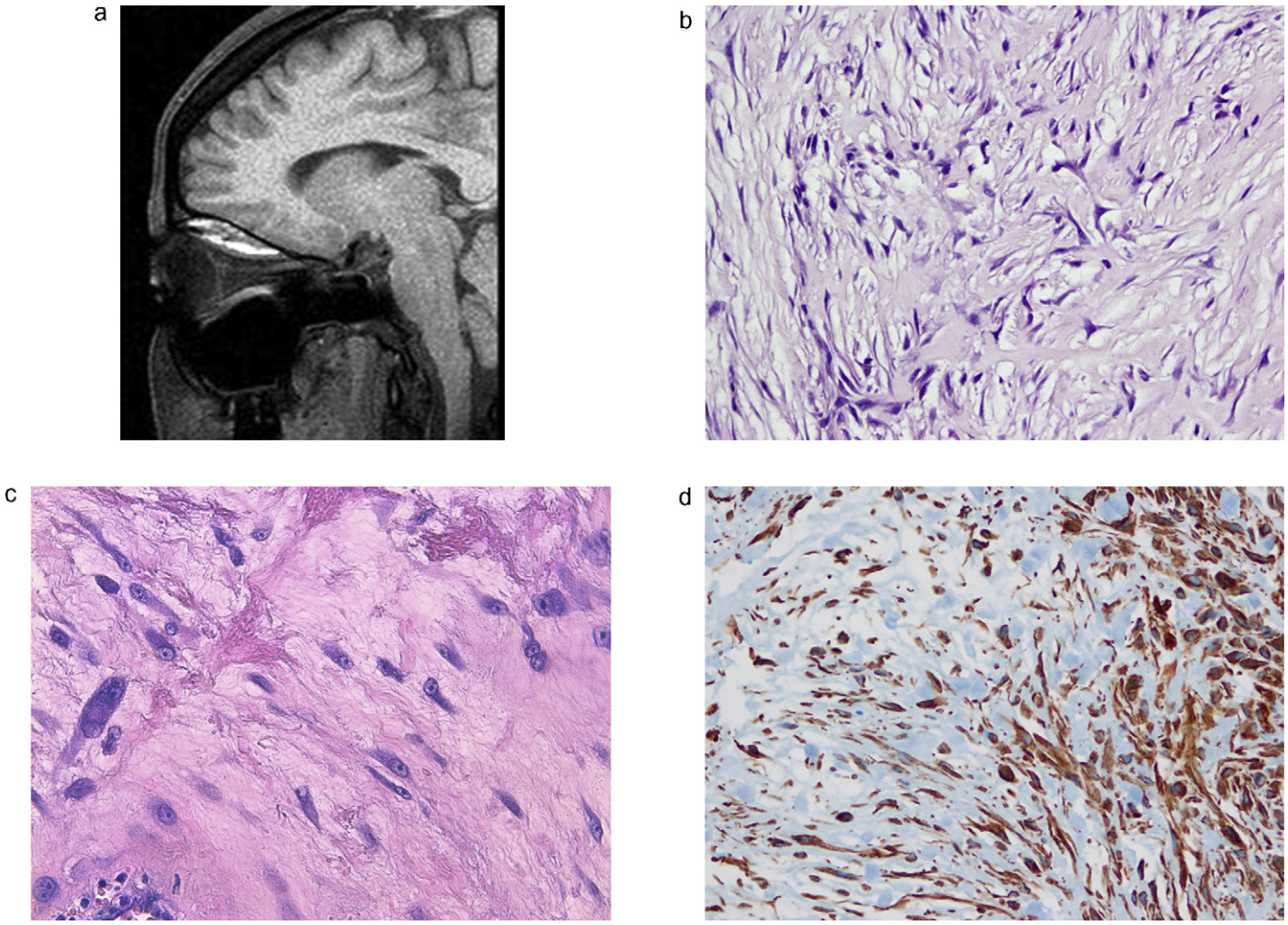

Fig. 1. (a) MRI of the orbital lesion before eye surgery in anteroposterior projection. At the upper quadrants of left eye-socket, a T2-weighted image shows a mass with iso-lower signal intensity, while it appears hypo-hyperintense in T1-weighted image. (b) Histological features of the orbital masses showing spindled-stellate cells, organized in areas with variable cellularity and areas of mixoid stroma (Hematoxylin-Eosin 270×). (c) Histological features of excised orbital masses showing ganglion-like cells with one or two nucleolated nuclei and large cytoplasm (Hematoxylin-Eosin 430×). (d) SMA (smooth muscle actin) immunostain showing cytoplasmic positivity of the cells (APAP 430×).

positivity for Desmin in spindled cells. Based on the histological and immunohistochemical findings, a diagnosis of PF was made. After surgery, the patient recovered well, and a post surgical MRI did not show any residual disease in the orbital cavity. Furthermore, two months later, she underwent a follow-up PET-CT scan, which was also negative. Eighteen months later, the patient returned to our attention, complaining of a subcutaneous nodule on the left arm. This lesion had first appeared one month earlier and had been slowly growing since then. At the clinical examination of the skin, there was a 1 cm hard mass, with no signs of inflammation, located at the volar side of the lower-third of the left forearm. The nodule was firm on subcutaneous tissue and painful at palpation. A left arm ultrasound showed a well-circumscribed nodule (max diameter 13 mm) with a mixed ultrasound pattern characterized by anecogenous areas intermingled with hyperecogenous septa (Fig. 2a). A Fine Needle Aspiration Cytology (FNAC) was performed on the nodule, and the cytological smears showed a pleomorphic, mainly dispersed, pattern of spindled and epithelioid cells and ganglion-like mesenchymal cells (Fig. 2b). The ganglion-like mesenchymal cells displayed prominent nucleoli, 1–2 central nuclei, and wide cytoplasm, resembling those of the primary orbital lesion (Fig. 2c). More than occasional mitoses were observed. The cytological diagnosis was mesenchymal proliferation consistent with PF. Because of the cytological diagnosis, a period of watchful waiting was suggested, but given its rapid growth, the presence of hypercellularity, cytological atypia, and mitotic activity, the lesion was surgically excised; the histopathological examination confirmed the cytological diagnosis of PF (Fig. 2d). Conventional immunostain, performed with the same monoclonal antibodies used for the previous orbital lesion, showed positivity for Vimentin, SMA, and Desmin, and negativity for CD34, bcl-2, S100, and Myogenin. Slides of the former orbital lesion were retrieved and microscopically evaluated with those of the latter, showing strict similarities between the two lesions. After 18 months, the patient is alive and well, without any signs of orbital or cutaneous relapse.

Discussion

Proliferative fasciitis is a pseudosarcomatous, benign proliferation of myofibroblasts with widely different anatomic locations, biological behavior, and pathological features [1]. The etiology is unknown, although a previous injury on the site of PF onset has been described in the literature. In our case, the patient did not recall any trauma, which is contrary to what was reported in some large series. In a PF series reported by Chung et al., 10 out of 53 patients had a history of trauma before PF, and Kiryu et al. also

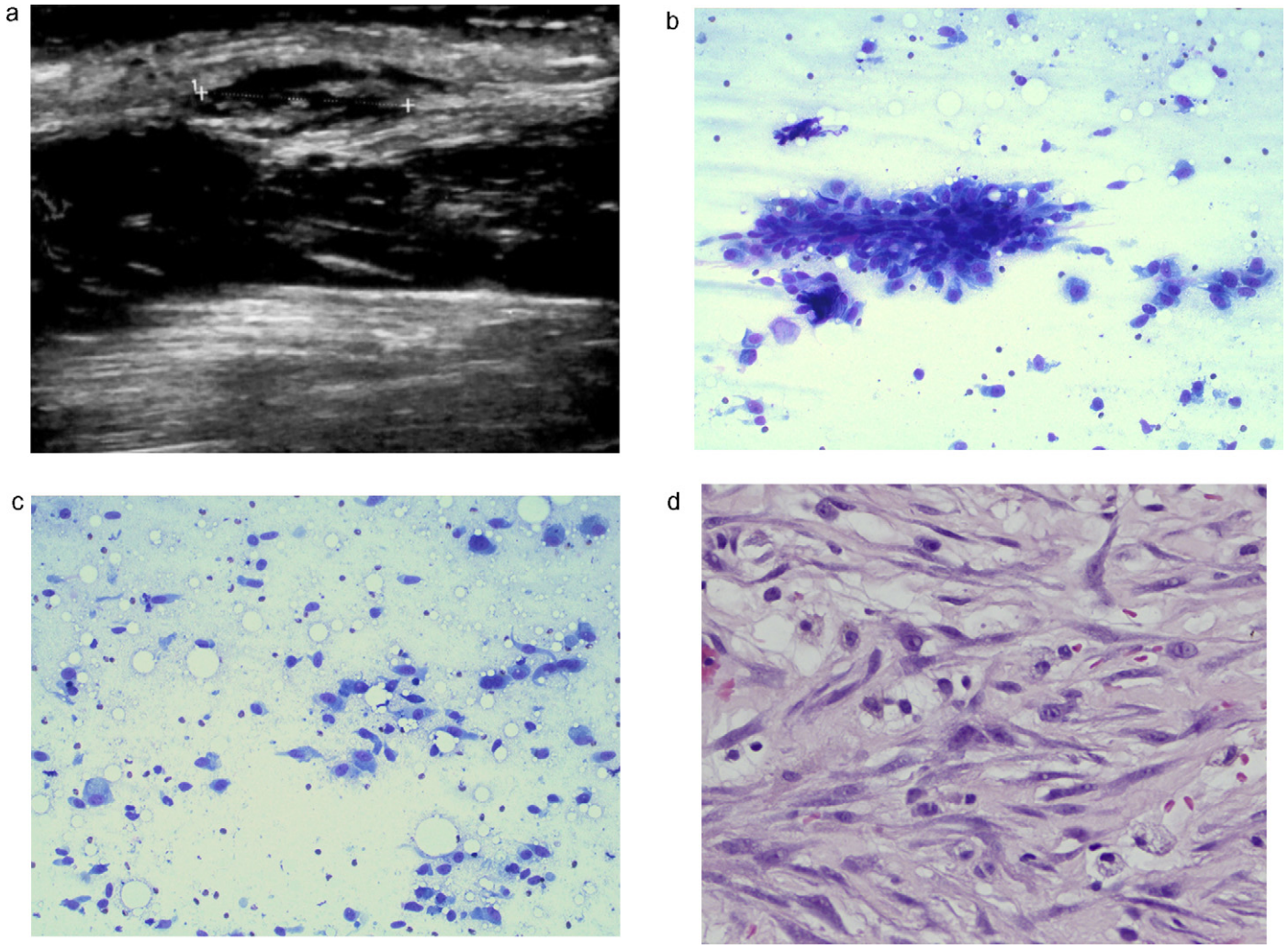

Fig. 2. (a) Ultrasound of left arm shows the presence in subcutaneous tissue of the volar aspect of the lower-third of left forearm of an oval encapsulated nodule (diameter 13 mm) with mixed echopattern characterized by anecogenous areas intermingled with hyperecogenous septa, without intralesional and perilesional signal flow. (b) A Fine Needle Aspiration smear of the arm's nodule showing aggregated and dispersed spindled and ganglion-like mesenchymal cells (Diff Quik Stain 270×). (c) Fine Needle Aspiration smear of the arm's nodule showing dispersed spindled and ganglion-like mesenchymal cells. The ganglion-like mesenchymal cells display central nuclei, prominent nucleoli, and wide cytoplasm, resembling those of the primary orbital lesion (Diff Quik Stain 270×). (d) Histological features of excised arm's nodule showing ganglion-like cells with one or two nucleolated nuclei and large cytoplasm; histological features showed strict similarities with the former orbital lesion (Hematoxylin-Eosin 430×).

described a case of PF arising adjacent to a surgical scar, suggesting that PF may be related to a reactive-reparative process [2,5].

PF is quite rare; PF cases described in the literature are summarized in Table 1; PF is equally distributed in both sexes and occurs predominantly in middle-aged adults (mean age, 51 years), although a rare variant in children has been reported. Its clinical presentation varies among patients. PF usually manifests itself, as in our case, as a firm, movable, often painful subcutaneous nodule with a size ranging from 0.5 to 11 cm. Honda et al. reported that 12 out of 20 patients with PF experienced pain at the site of the lesion, and Chung reported that tenderness or pain was present in about two-thirds of his patients [2,6–10]. The upper extremities are the most common site of onset for PF (37 cases among the 102 described in the literature), especially the volar side of forearm, followed by the lower extremities (33 cases), trunk (24 cases), head and neck (7 cases).

The diagnosis always depends on the pathological examination. PF forms a poorly circumscribed mass in subcutaneous tissue and may extend horizontally along the fascia. Microscopically, the histological finding consists of fibro-myofibroblastic spindle-shaped cells, intermingled with large ganglion-like cells with large rounded regular nuclei, prominent nucleoli, dispersed chromatin, and abundant basophilic or amphophilic cytoplasm. A variable number of bi-nucleate and multinucleated giant cells may also be found, presenting a patchy distribution. Mitotic figures are very frequent in both cells and may be relatively numerous. Rarely atypical mitotic figures can be encountered. This worrisome feature should not be confused with a sign of malignancy [1,15].

The stroma varies from mixoid to collagenous. Focal necrosis and acute inflammation may be present. The immunohistochemical profile of PF is characterized by positivity for smooth muscle actin (SMA) and muscle-specific actin (MSA), vimentin, fibronectin, variable for CD68, and by negativity for S100 in spindled-stellate cells. In addition, ganglion-like cells may stain only focally or weakly for actins whereas they are negative for desmin, S100, neuron-specific enolase, and keratin [2–6]. DNA flow cytometric analyses of proliferative fasciitis show a uniformly diploid pattern although one case of trisomy 2 has been described, suggesting that these processes might be the result of clonal cell proliferation [11,12].

Although the histological examination by core biopsy or excision is the gold standard for an accurate diagnosis, FNAC performed by experienced cytologists is also an acceptable method to characterize the lesion [8]. However, in this case, a very careful

Table 1
Proliferative fasciitis: a review of the literature.

	No. of cases	Median age (range)	Sex	Site of Onset: no. of cases (%)	Maximum size (range)	Spontaneous resolution	Recurrence
Chung et al. [2]	53	54 (22–78)	28 M 25 F	Upper extremities 22 (41%) Lower extremities 17 (32%) Trunk 12 (23%) Head 1 (2%) Not specified 1 (2%)	6 cm (0.4–6 cm)	No	Yes (1 case)
Lundgren et al. [3]	4	54 .5 (46–60)	1 M 3 F	Abdominal wall 1 (25%) Chest wall 1 (25%) Left groin 1 (25%) Back 1 (25%)	5 cm (1.5–5 cm)	Yes (1 case)	No
Meis and Enzinger [4]	11	7 (0.21–13)	9 M 2 F	Lower extremities 5 (45%) Upper extremities 3 (27%) Head and neck region 2 (18%) Chest wall 1 (10%)	1.5–11 cm	Yes (1 case)	Yes (1 case)
Kiryu et al. [5]	1	61	1 M	Right lower leg 1 (100%)	3 cm	No	No
Diaz-Flores et al. [6]	2	57 .5 (52–63)	2 M	Trunk 1 (50%) Right leg 1 (50%)	4 cm (3–4 cm)	No	No
Honda et al. [7]	20	60 (20–75)	11 F 9 M	Lower extremities 8 (40%) Upper extremities 6 (30%) Trunk 4 (20%) Head–neck 2 (10%)	N.A.	No	No
Wong [8]	2	34 .5 (34–35)	1 F 1 M	Right arm 1 (50%) Neck 1 (50%)	1.2 cm (1–1.2 cm)	Yes (1 case)	No
Ushigome et al. [9]	2	51 (51)	1 F 1 M	Left mandibular region 1 (50%) Chest wall 1 (50%)	2.5 cm (1.6–2.5 cm)	No	No
Lorenc et al. [10]	1	7	1 F	Left palm 1 (100%)	3 cm	No	No
Dembinski et al. [11]	1	82	1 M	Left buttock 1 (100%)	3.3 cm	No	No
Kato et al. [13]	1	35	1 F	Forearm 1 (100%)	4 cm	Yes	No
Magro et al. [15]	1	13	1 M	Retroauricolar 1 (100%) region	2.5 cm	No	No
Richards et al. [16]	1	19	1 M	Finger 1 (100%)	1.5 cm	No	No
Sasano et al. [17]	1	56	1 M	Left forearm 1 (100%)	1.5 cm	No	No
Morgan et al. [18]	1	7	1 F	Right forearm 1 (100%)	2 cm	No	No

N.A., not available; M, male; F, female.

observation was necessary, given the wide cytological overlap between PF and sarcoma [2,3,5].

As far as the biological behavior is concerned, PF usually has a self-limited course, and spontaneous resolution has been reported in most of the series published [3,4,8,13]. The lesion usually disappears within 1–12 weeks (mean 4.7 weeks) after the preoperative diagnosis by FNAC and does not recur [8]. Nonetheless, because of its rapid growth, PF resembles a malignant tumor, especially when located in deep anatomic districts where it seems to grow even faster and to reach a larger size. Moreover, recurrences in the sites of a previous excision have also been described, mainly in deeply located PF. Therefore, because of the clinical behavior and the microscopic similarities of PF and sarcoma, the most relevant problem for patients with PF is over-treatment due to a misdiagnosis. PF usually manifests itself as a single lesion: in fact, although pseudosarcomatous diseases, such as multifocal proliferative myositis and nodular fasciitis, have been previously reported in the literature, multifocal proliferative fasciitis has never been previously described [14].

Recurrence of PF after primary excision is unusual. In the literature, only 2 cases have been described so far [2,4]. In both patients, recurrences were located at the site of the initial lesion and were successfully treated by local excision. Despite the possibility of local recurrence, to the best of our knowledge, cases of multiple PF arising in different anatomic sites have never been previously reported. This occurrence does not allow any conclusion on the nature of PF whereas it seems to support the possibility of a clonal rather than a reactive process.

References

[1] C.D.M. Fletcher, K.K. Unni, F. Mertens, Pathology and Genetics of Tumours of Soft Tissue and Bone. World Health Organization Classification of Tumours, WHO, 2002.
[2] E.B. Chung, F.M. Enzinger, Proliferative fasciitis, Lancet 36 (1975) 1450–1458.

[3] L. Lundgren, L.G. Kindblom, J. Willems, U. Falkmer, L. Angervall, Proliferative myositis and fasciitis. A light and electron microscopic, cytologic, DNA-cytometric and immunohistochemical study, APMIS 100 (1992) 437–448.
[4] J.M. Meis, F.M. Enzinger, Proliferative fasciitis and myositis of childhood, Am. J. Surg. Pathol. 16 (1992) 364–372.
[5] H. Kiryu, H. Takeshita, Y. Hori, Proliferative fasciitis. Report of a case with histopathologic and immunohistochemical studies, Am. J. Dermatopathol. 19 (1997) 396–399.
[6] L. Diaz-Flores, A.I. Martin Herrera, R. Garcia Montelongo, R. Gutierrez Garcia, Proliferative fasciitis: ultrastructure and histogenesis, J. Cutan. Pathol. 16 (1989) 85–92.
[7] Y. Honda, T. Oh-I, M. Koga, H. Serizawa, A case of proliferative fasciitis in abdominal region, J. Dermatol. 28 (2001) 753–758.
[8] N.L. Wong, Fine needle aspiration cytology of pseudosarcomatous reactive proliferative lesions of soft tissue, Acta Cytol. 46 (2002) 1049–1905.
[9] S. Ushigome, T. Takakuwa, M. Takagi, H. Koizumi, M. Morikubo, Proliferative myositis and fasciitis. Report of five cases with an ultrastructural and immunohistochemical study, Acta Pathol. Jpn. 36 (1996) 963–971.
[10] Z.P. Lorenc, S. Brourman, J.E. Imbriglia, Proliferative fasciitis of the hand in a child, J. Hand Surg. Am. 12 (1987) 1066–1070.
[11] A. Dembinski, J.A. Bridge, J.R. Neff, C. Berger, A.A. Sandberg, Trisomy 2 in proliferative fasciitis, Cancer Genet. Cytogenet. 60 (1992) 27–30.
[12] E.N. McComb, J.R. Neff, S.L. Johansson, M. Nelson, J.A. Bridge, Chromosomal anomalies in a case of proliferative myositis, Cancer Genet. Cytogenet. 98 (1997) 142–144.
[13] K. Kato, S. Ehara, J. Nishida, T. Satoh, Rapid involution of proliferative fasciitis, Skeletal Radiol. 33 (2004) 300–302.
[14] L.V. Nagaraj, W. Fangman, W.L. White, J.T. Woosley, N. Prose, A. Selim, D.S. Morrell, Self-healing juvenile cutaneous mucinosis: cases highlighting subcutaneous/fascial involvement, J. Am. Acad. Dermatol. 55 (2006) 1036–1043.
[15] G. Magro, M. Michal, R. Alaggio, E. D'Amore, Intradermal proliferative fasciitis in childhood: a potential diagnostic pitfall, J. Cutan. Pathol. 38 (2011) 59–62.
[16] R.H. Richards, G. Evans, J.A. Fitzgerald, G.H. Millward-Sadler, Proliferative fasciitis of a finger: a case report, J. Hand Surg. Br. 15 (1990) 501–502.
[17] H. Sasano, H. Yamaki, Y. Ohashi, S. Ohtsuki, H. Nagura, Proliferative fasciitis of the forearm: case report with immunohistochemical, ultrastructural and DNA ploidy studies and a review of the literature, Pathol. Int. 48 (1998) 486–490.
[18] K. Morgan, G. Batcup, S. Aparicio, R.D. Spicer, H.B. Marsden, Proliferative fascitis in childhood: a case report, Pediatr. Pathol. 10 (1990) 431–438.