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EDITORIAL COMMENTARY

Rare but Perils of Unaware - Fibrodysplasia Ossificans Progressiva

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In this issue of IJP, Gupta et al. have published a series of 12 patients with an autosomal dominant genetic disorder, fibrodysplasia ossificans progressiva (FOP) [1]. This study is unique as it reports a misdiagnosis of upto 60%, and highlights the unmet need for increasing awareness of the primary care physicians for genetic disorders. FOP was first recognized by an English surgeon in 1736, and in 1868, referred to as myositis ossificans progressiva when the great toe abnormalities were included. Harry Eastlack, born in 1933, donated his fused skeleton in Philadelphia's Mutter Museum as a witness of the impact of trauma and multiple surgical interventions towards heterotopic bone formation in this disorder [2]. Despite the fact that FOP has been recognized for so long in literature, the authors report a diagnostic delay of upto 15.5 y, inspite of onset of disabling osseous manifestations starting as early as one to seven years of life. This is not uncommon for rare disorders which require ongoing education to decrease diagnostic odysseys of patients and families.

For the diagnosis of FOP, a characteristic clinical clue is the malformed great toe since birth, hallux valgus with malformed first metatarsal and fused inter phalangeal joint [3]. The authors report this in all but one patient and assert the importance of this malformation along with heterotopic calcification to allude to a diagnosis of FOP. A simple test for the common variant, c.617G>A;p.Arg206His, in *ACVR1* gene confirms the diagnosis. Additional skeletal developmental abnormalities and joint degeneration are reported [4].

The precursors of heterotopic soft tissue calcification are "flare-ups", which are hallmarks of the disease. These are painful, soft tissue swellings associated with stiffness and decreased range of joint motion. They are commonest in the back, lower spine and abdomen. Flares result in heterotopic calcification of skeletal muscles, tendons, fascia and ligaments in about 50% patients and complete resolution in very few. Recurrent flare-ups were reported in 83% patients in the current study with heterotopic ossification in all. Trauma, viral infection, incisions, intramuscular injection and invasive procedures like biopsies, induce catastrophic and painful new bone deposition in patients. It is important to prevent iatrogenic ossification through IM administration of immunization and unnecessary biopsies [5]. There is a crucial role of early diagnosis of FOP to prevent avoidable and harmful procedures and also unnecessary medications as received by seven patients in the current study.

Misdiagnosis for FOP is well reported and the authors too bring this to attention [1, 2]. Differential diagnosis include congenital toe malformations, hereditary multiple osteochondromas, progressive osseous heteroplasia and neoplasms. The combination of bilateral hallux malformation with heterotopic ossification and flare-ups are typical of FOP, not seen in other disorders.

With increasing availability of definitive treatment for rare disorders, an early diagnosis is important for better outcomes. Palovarotene is recently FDA approved for treatment of FOP, predominantly targeting new bone formation but long term data of safety and efficacy are underway [6]. However, this is a hope for patients with this life-limiting disease.

Declarations

Conflict of Interest None.

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