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CASE BASED REVIEW

Isotretinoin-induced sacroiliitis in patients with hidradenitis suppurativa: a case-based review

Belkıs Nihan Coskun[1] · Burcu Yagiz[1] · Yavuz Pehlivan[1] · Ediz Dalkilic[1]

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Abstract

Hidradenitis suppurativa (HS) is a chronic, suppurative skin disease characterized by painful nodules, particularly in the axillae and groin. Isotretinoin can be used in the treatment of HS; however, it may paradoxically lead to skin lesions or worsen the existing lesions. Isotretinoin, which is commonly used in the treatment of severe acne, is associated with several side effects, including rheumatic side effects and rarely sacroiliitis. In this study, we discussed two cases who presented with low back pain after isotretinoin was used for the treatment of acne vulgaris. The patients did not have low back pain before isotretinoin use and did not have enthesitis, dactylitis, uveitis, psoriasis, recent infection, trauma, and family history spondylitis. HLA-B27 was negative. Bone-marrow edema was detected at the sacroiliac joint on magnetic resonance imaging. Because of these findings, sacroiliitis related to the drug was considered in our patients and isotretinoin treatments were discontinued. Because the patients' low back pain continued when they administered non-steroidal anti-inflammatory drugs, biological drug treatments were started. Both cases presented had a simultaneous HS lesion. After the treatment, both low back pain and HS lesions regressed. Patients with isotretinoin therapy should be alerted for inflammatory low back pain and HS lesions that may develop. We should note that biologic agents should be considered in the treatment of resistant cases.

Keywords Acne · Hidradenitis suppurativa · Isotretinoin · Sacroiliitis

Introduction

Hidradenitis suppurativa (HS) is a chronic, suppurative skin disease characterized by involvement of the apocrine glands in different body regions, particularly the axillae and groin, and mostly affects young females. HS typically presents with recurrent abscesses, sinus tract formation, and scaring. The diagnosis of HS is made clinically using lesion morphology and location. Medical treatment includes topical and systemic antibiotics, intralesional steroid injection, systemic retinoids, hormone therapies, systemic immunomodulators, and biological agents [1, 2].

Isotretinoin is a systemic retinoid mainly used to treat severe and recalcitrant nodulocystic acne and HS as well. However, HS is associated with a wide range of side effects on the reproductive system, skin, ocular, neurological, hepatic, and musculoskeletal system [3–5]. The most frequent rheumatic side effects of retinoids include myalgia, arthralgia, peripheral arthritis, low back pain, and sacroiliitis, which account for about 20% of cases [6].

In the literature, several case reports of isotretinoin-induced sacroiliitis have been described [6–26]. NSAIDs were commonly used for the treatment of these cases successfully. In the relevant literature, only one patient had received biologic treatment [8]. Isotretinoin-induced sacroiliitis or isotretinoin-induced HS was present, but there were not any cases with both isotretinoin-induced sacroiliitis and isotretinoin-induced HS.

Herein, we report two cases who received isotretinoin for acne vulgaris and developed bilateral sacroiliitis and HS lesions. We discussed biological treatment in our cases in light of the current literature.

✉ Belkıs Nihan Coskun
belkisnihanseniz@hotmail.com

Burcu Yagiz
burcuyilmaz_84@hotmail.com

Yavuz Pehlivan
drypehlivan@gmail.com

Ediz Dalkilic
edizinci@hotmail.com

[1] Division of Rheumatology, Bilim Dalı, Uludağ Üniversitesi Tıp Fakültesi Romatoloji, Görükle, Nilüfer, 16059 Bursa, Turkey

Case presentation

Case 1

A 20-year-old female patient who was treated with isotretinoin for cystic acne vulgaris for 6 months was admitted with nocturnal low back pain, morning stiffness, limited range of motion (ROM) of the hip joint, and fatigue for 5 months with increasing severity. She had no history of chronic, inflammatory, low back pain before isotretinoin treatment. The patient declared no history of infection and trauma recently. In addition, she denied any family history of spondyloarthritis. There was no history of enthesopathy, peripheral joint involvement, ocular findings, and psoriatic lesions. Physical examination showed positive sacroiliac compression testing and positive Patrick's Fabere test with painful and limited ROM of the hip joint. Her medical history revealed erythematous nodules located in the axilla and groin for 3 months. On her dermatological examination, HS was diagnosed. Laboratory test results were within normal ranges and human leukocyte antigen (HLA)-B27 was negative. Brucella rose bengal was negative. Plain X-ray was normal. Bone-marrow edema was detected on magnetic resonance imaging (MRI) on STIR (short tau inversion recovery) in bilateral sacroiliac joints, consistent with active sacroiliitis. History, laboratory and imaging studies indicated a 'drug-induced sacroiliitis.'

Although the patient was not diagnosed as Ankylosing Spondylitis, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score was used to measure disease activity due to lack of any specific index for drug-induced sacroiliitis. Her BASDAI score was 9, indicating severe disease activity. Despite medical treatment with three different nonsteroidal anti-inflammatory drugs (NSAIDs) in maximal doses (Diclofenac 150 mg/day, indomethacin 150 mg/day, acemetacin 120 mg/day, respectively), pain relief was unable to be achieved. Therefore, the patient was initiated on infliximab, which is a chimeric monoclonal antibody. On 6-week follow-up, she declared a significant relief of pain and the BASDAI score was decreased to 2. The infliximab 300 mg infusion was planned to be administered in every 6 weeks. It was observed that HS lesions were regressed.

We tried to decrease the frequency of infusions; however, the patient suffered from increased pain. Up to date, she has received 10 cycles of infliximab 300 mg infusion in 6–8 weeks.

Case 2

A 27-year-old male patient who was treated with isotretinoin for cystic acne vulgaris for 6 months was admitted with nocturnal low back pain, morning stiffness, and fatigue for 4 months with increasing severity. He had no history of chronic, inflammatory, and low back pain before isotretinoin treatment. The patient declared no history of infection and no trauma. In addition, she has no family history of spondyloarthritis. There was no history of enthesopathy, peripheral joint involvement, ocular findings, and psoriatic lesions. Physical examination showed positive sacroiliac compression testing and positive Patrick's Fabere test with painful ROM of the hip joint. His history revealed erythematous nodules and scars located in the axilla and groin and skin lesions were present for 3–4 years, which worsened following isotretinoin treatment. On his dermatological examination, HS was diagnosed. His laboratory test results showed an erythrocyte sedimentation rate of 17 mm/h and a C-reactive protein (CRP) of 1.3 mg/dL. The HLA-B27 was negative. Brucella rose bengal was negative. Plain X-ray showed a narrowing of the bilateral sacroiliac joint widths. On MRI (on STIR), bone-marrow edema was detected in bilateral sacroiliac joints. These findings were consistent with active sacroiliitis. History, laboratory, and imaging studies indicated that a 'drug-induced sacroiliitis.' His BASDAI score was 6.5, indicating active disease. Despite medical treatment with three different NSAIDs in maximal doses (Diclofenac 150 mg/day, indomethacin 150 mg/day, naproxen 750 mg/day, respectively), pain relief was unable to be achieved. As the patient was unresponsive to NSAIDs with increased HS lesions, he was initiated on adalimumab, which is a fully human anti-tumour necrosis factor α monoclonal antibody. Following treatment for 2 years, the patient suffered from increasing low back pain and morning stiffness for longer than 2 h with elevated acute phase reactants, and he was switched from adalimumab to infliximab with the suspicion of secondary unresponsiveness. 12 weeks after the initiation of the therapy, he declared a significant relief of pain and the BASDAI score was decreased to 3.5. The patient is still under follow-up on infliximab for 1 year and is free from low back pain and HS skin lesions.

Search strategy

Case-based review strategy was applied according to the recommendations by Gasparyan et al. [27] who recommended that at least 2–3 credible databases, selective to provide high-quality and current studies. We searched, MEDLINE/PubMed; Web of Science and Scopus databases using MeSH terms "sacroiliitis" [AND] "isotretinoin" until July 13, 2019.

Only case reports and clinical studies covering isotretinoin-related sacroiliitis were included to this review [6–26] Reviews, articles, including SAPHO and any other irrelevant articles, reporting not about isotretinoin-related sacroiliitis

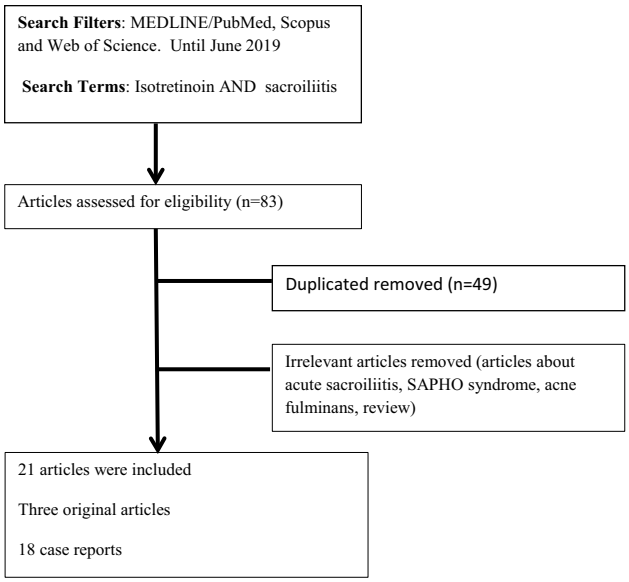

Fig. 1 Flowchart of the search strategy of the review

were excluded. The flow chart demonstrating the search strategy of our study is presented in Fig. 1.

Discussion

Isotretinoin is one of the most potent agents in the treatment of acne; however, it may paradoxically lead to worsening of existing lesions and joint involvement. In this paper, we presented the management of our two cases who were referred with the complaint of severe low back pain and diagnosed as drug-induced sacroiliitis, while they were on isotretinoin treatment. Our search criteria revealed a total of 21 publications on isotretinoin-induced sacroiliitis, including 18 case reports ($n=46$). [6–26]. Demographic and clinical characteristics of these reports in the literature and our cases are summarized in Table 1. As distinct from the other reported cases, our cases had bilateral HS lesions in the axilla and groin region.

Currently, the exact prevalence of drug-induced sacroiliitis is unknown. However, in a recent prospective study, spondyloarthropathy was seen in 23.1% of patients treated with isotretinoin [12]. In a study, including 73 patients, Baykal et al. [6] reported the prevalence of isotretinoin-induced sacroiliitis as 8.2% and isotretinoin-induced low back pain as 21.9%. In addition, arthritis accompanied by sacroiliitis was reported in 21% of patients with acne fulminans [11]. Sacroiliitis may also develop secondary to isotretinoin used to treat acne fulminant [25, 26].

Isotretinoin-induced rheumatic symptoms include bilateral and unilateral sacroiliitis, acute arthritis, enthesopathy, inflammatory low back pain, polyneuropathy, and myopathy. Although rare, peripheral arthritis has also been reported. The most frequent involvement sites are wrist, metacarpophalangeal joints, knee, elbow, and hip [8, 13, 22, 28–30]. Both our cases were presented low back pain. Our literature search revealed that low back pain was the main presenting symptom in 66.6% of the cases.

Although the link between isotretinoin a sacroiliitis has been not recently described, it is not fully covered. In one of the earlier researches, Huges et al. found non-inflammatory characterized synovial fluid in their patient with isotretinoin-induced sacroiliitis, suggesting that retinoids may result in immune dysfunction (such as an alteration of the cytokine balance), thereby, leading to arthritis and vasculitis. [31] In addition, it has been proposed that isotretinoin makes the cells vulnerable to minor traumas, which are not typically associated with significant diseases [31]. The underlying mechanism is that isotretinoin induces lysosomal membrane solubilization and disrupts the synovial cells cytopathically, leading to arthritis [32].

Cell-mediated autoimmunity due to isotretinoin hypersensitivity has also been blamed for the multiple target involvement [33]. In a study, interleukin (IL)-1α, IL-1β, and tumour necrosis factor (TNF)-α levels decreased in patients receiving isotretinoin treatment [34]. TNF-α, IL-17, IL-32, IL-36, and various other mediators are believed to be play a role in HS pathogenesis. However, the most potent mediator responsible for emerging of the disease is still elusive [35]. We speculate that the decrease in TNF-α by retinoids is not sufficient enough to control the disease because of the other mediators' effects. Retinoids are expected to have fewer deleterious effects and even more beneficial effects in spondyloarthritis (SpA) in low doses. In a study, Bidad et al. [36] showed that all-trans retinoic acid decreased TNF-α secretion in ankylosing spondylitis. A clinical study demonstrated that retinoids increased matrix metalloproteinase 2 (MMP-2) [37]. MMP-2 increase may also cause arthritis by causing synovial synovial membrane damage [38]. Retinoic acid can activate matrix metalloproteinase 2 (MMP-2), causing synovial membrane degradation in joints.

When the causes of acute sacroiliitis are examined, pyogenic sacroiliitis was reported as the most common reason. Pyogenic sacroiliitis usually develops after intravenous drug use, skin infections, infective endocarditis, and pregnancy. Other causes of acute sacroiliitis include acute brucella sacroiliitis, gout, and calcium pyrophosphate dihydrate (CPPD) deposition , drug-induced sacroiliitis, and malignant disorders [39]. Synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome is considered a member of spondyloarthropathy family which may present with unilateral or bilateral sacroiliitis and its association with HLA-B27 is unknown [40]. In our both cases, SAPHO syndrome was ruled out, as the skin lesions are ulcerated, although rarely nodulocystic. In addition, there was no evidence of

Table 1 Demographic and clinical characteristics of cases reported in the literature and our cases

	Author, years	Sex, age (years)	Complaints on admission	HLA-B27	Radiographic signs	Treatment
	Coşkun (2019)	F, 20	LBP	Negative	MRI: bilateral SI	Infliximab
	Coşkun (2019)	M, 27	LBP	Negative	MRI: bilateral SI	Adalimumab Infliximab
1	Aydog [7]	7 M, 2F[a]	LBP, hip pain,	4 Positive 5 Negative	MRI: bilateral SI	NSAID Sulfasalazine Prednisolone
2	Dawoud [8]	M, 16	LBP	Negative	MRI: bilateral SI and synovitis of the hip	Adalimumab
3	Kocak [9]	3 M, 8F[a]	Bilateral hip pain	Negative	MRI: Mild SI $n=5$ Moderate SI $n=4$ Severe SI $n=2$	Indomethacin (colchicine, $n=1$)
4	Baykal [6]	1 M, 5F[a]	LBP	Unknown	MRI: bilateral SI (in male) Unilateral SI (in females)	NSAID
5	Yıldızgoren [10]	F, 32	LBP	Negative	MRI: bone-marrow edema	Indomethacin
6	Rodriguez [11]	M, 14	LBP, hip pain, fever	Negative	MRI: bilateral multifocal SI	Prednisolone MTX
7	Alkan [12]	F	LBP	Negative	MRI: unilateral SI	NSAID
8	Tasdelen [13]	M, 23	Painful wrist and MCP joints	Negative	MRI: Left-sided active SI	Naproxen Sulfasalazine Prednisolone
9	Cakır [14]	M, 23	LBP	Negative	MRI: bone-marrow edema	Not available
10	Geller [15]	M, 18	Fever, arthralgia	Negative	Scintigraphy: mild bilateral SI	NSAID
11	Yılmazer [16]	F, 20	Arthralgia, myalgia	Positive	MRI: bone-marrow edema	Diclofenac Prednisolone
12	Levinson [17]	M, 17	LBP	Negative	MRI: bilateral SI and bone-marrow edema	Naproxen
13	Zanelato [18]	M, 14	LBP, hip pain, rib pain	Negative	Scintigraphy: mild bilateral SI	Prednisolone Acetaminophen
14	Barbareschi [19]	M, 17	Fever, fatigue, arthralgia	Negative	X-ray: widening and erosion of left-sided sacroiliac joint	NSAID Sulfasalazine Prednisolone
15	Rozin [20]	M, 28	LBP, hip pain	Negative	Scintigraphy: increased involvement in SI joint MRI: diffuse subarticular edema	ACTH repository injection Etodolac
16	Gultepe [21]	M, 27	LBP	Negative	X-ray: bilateral SI	NSAID Sulfasalazine
17	Ekşioğlu [22]	M, 20	Bilateral hip pain	Positive	MRI: diffuse subarticular edema	Naproxen
18	Dincer [23]	2 M, F[a]	LBP	2 Negative 1 Positive	MRI: bone-marrow edema Scintigraphy: increased involvement in SI joint	NSAID
19	Atabek [24]	M, 14	LBP	Negative	MRI: bilateral SI	Sulfasalazine Prednisolone
20	Bachmeyer [25]	M, 17	Hip pain, gait abnormality	Negative	X-ray: widening and erosion of sacroiliac joints Scintigraphy: Increased involvement in SI joint	Piroksikam Piroxicam Prednisolone
21	Elias [26]	M, 17	LBP	Negative	X-ray: asymmetric, bilateral SI, calcaneitis	Prednisolone Indomethacin

SI sacroiliitis, *MTX* methotrexate, *MCP* metacarpophalangeal, *LBP* low back pain, *MRI* magnetic resonance imaging, *NSAID* non-steroidal anti-inflammatory drug

[a]Multiple cases were reported

radiographic hyperostosis and osteitis despite the presence of systemic symptoms and inducible factor (isotretinoin). There was no history of low back pain before isotretinoin use, and there was no history of peripheral arthritis, enthesitis, dactylitis, uveitis, psoriasis, recent infection, fever, weight loss, trauma, and family spondylitis. Brucella rose bengal negative, complete blood count, routine biochemistry tests, and uric acid were found to be normal in laboratory tests. In light of all these findings, we considered drug-induced sacroiliitis in our patients and discontinued isotretinoin treatments.

Drug-induced sacroiliitis typically develops acutely days or weeks after the initiation of isotretinoin. Sacroiliac pain usually manifests with mild-to-moderate ESR and CRP elevation and progress to bone-marrow oedema of the sacroiliac joint as assessed by MRI. The positivity of HLA-B27 is thought to make the patient susceptible to sacroiliitis [22]. On the other hand, there are several reports which contradict this view in the literature [3, 4, 6, 8, 9, 11]. In their case series, Pehlivan et al. [41] reported four cases with isotretinoin-related inflammatory low back pain and none of them showed HLA-B27-positivity. Similarly, our both cases were HLA-B27 negative. One patient had moderate CRP. MRI showed bone-marrow oedema of the sacroiliac joint in both patients. Although isotretinoin-induced arthritis is a self-limiting disease in a short time period or controlled with NSAIDs, there are several reports with long-term persistence in the literature.

Recovery may take several months after the discontinuation of treatment. Glucocorticosteroids and NSAIDs are useful in the treatment of acute symptoms [6]. In the majority of cases reported in the literature, clinical symptoms relieved after the discontinuation of isotretinoin and addition of NSAIDs [6, 8, 12, 15, 17, 22]. All these cases were treated with NSAIDs, while ten with prednisolone, five with sulfasalazine, and one with adalimumab.

In their study, Bachmeyer et al. [25] re-administered isotretinoin at a dose of 0.1 mg/kg/day for a couple of weeks and relapsing pain was observed at 48 h. Therefore, prednisolone was combined with isotretinoin treatment at a dose of 0.5 mg/kg/day. In another report, Barbareschi et al. [19] described a case of unilateral sacroiliitis induced by isotretinoin treatment. Once isotretinoin was discontinued, symptoms relieved, and completely resolved over time. Of note, Yilmazer et al. [16], Elias et al. [26], and Bachmeyer et al. [25] added prednisolone to the NSAID treatment (15 mg/day, 30 mg/day, and 30 mg/day, respectively). In another study, Tasdelen et al. [13] and Barbareschi et al. [19] combined sulfasalazine with prednisolone and NSAIDs for disease remission. In addition, Zanelato et al. [18] re-initiated prednisolone 30 days after the discontinuation of isotretinoin.

In the study of Yilmazer et al. [16] and Barbareschi et al. [19], treatment duration with low-to-moderate dose oral steroids and NSAIDs ranged from 6 weeks to 1 year. Levinson [17] and Eksioglu [22] used only oral NSAIDs for the treatment of sacroiliitis, and symptomatic relief was achieved within a few weeks. In another study, isotretinoin-induced peripheral arthritis was mostly treated with isotretinoin discontinuation and NSAID treatment for a few months [29, 30]. In our both cases, we discontinued isotretinoin and initiated NSAIDs; however, an anti-TNF-α was selected due to treatment unresponsiveness.

Although the exact pathogenesis of HS has not been clearly elucidated yet, in a recent study, biopsy specimens were obtained from HS lesions and, compared to normal skin specimens, a reduction or absence of sebaceous glands was seen in HS patients, which might contribute to the pathogenesis of the disease [1, 42]. More importantly, the main effect of isotretinoin was to decrease the size and action of sebaceous glands, and therefore, isotretinoin reduced the sebaceous glands and could potentially worsen HS. Although isotretinoin is used in the treatment of HS, it may paradoxically lead to worsening of existing lesions in certain cases. Consistent with this finding, Gallagher et al. [43] reported that patients with acne in whom isotretinoin would be initiated should be evaluated for HS. In one of our cases, isotretinoin-induced new HS lesions, while it worsened the existing lesions in the other case. The association between HS and musculoskeletal symptoms has rarely been reported [44–47].

In conclusion, acute sacroiliitis and HS are rare complications of isotretinoin treatment. Although rarer than sacroiliitis development, HS can be activated with isotretinoin, and thus, clinicians should be alert for HS during the initiation and follow-up of isotretinoin treatment. In NSAIDs' refractory cases, TNF blockers can provide pain relief and diminish of the cutaneous lesion.

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Compliance with ethical standards

Conflict of interest All authors declare no conflict of interest.

Informed consent Informed consent was obtained from our patients included in this study.

References

1. Frew JW, Hawkes JE, Krueger JG (2019) Topical, systemic and biologic therapies in hidradenitis suppurativa: pathogenic

insights by examining therapeutic mechanisms. Ther Adv Chronic Dis 10:2040622319830646
2. Saunte DML, Jemec GBE (2017) Hidradenitis suppurativa: advances in diagnosis and treatment. JAMA 318(20):2019–2032
3. Zaenglein AL, Pathy AL, Schlosser BJ, Alikhan A, Baldwin HE, Berson DS, Bowe WP, Graber EM, Harper JC, Kang S, Keri JE, Leyden JJ, Reynolds RV, Silverberg NB, Stein Gold LF, Tollefson MM, Weiss JS, Dolan NC, Sagan AA, Stern M, Boyer KM, Bhushan R (2016) Guidelines of care for the management of acne vulgaris. J Am Acad Dermatol 74(5):945–973.e933
4. Strauss JS, Krowchuk DP, Leyden JJ, Lucky AW, Shalita AR, Siegfried EC, Thiboutot DM, Van Voorhees AS, Beutner KA, Sieck CK, Bhushan R, American Academy of Dermatology/American Academy of Dermatology A (2007) Guidelines of care for acne vulgaris management. J Am Acad Dermatol 56(4):651–663
5. Tripathi SV, Gustafson CJ, Huang KE, Feldman SR (2013) Side effects of common acne treatments. Expert Opin Drug Saf 12(1):39–51
6. Baykal Selcuk L, Aksu Arica D, Baykal Sahin H, Yayli S, Bahadir S (2017) The prevalence of sacroiliitis in patients with acne vulgaris using isotretinoin. Cutan Ocul Toxicol 36(2):176–179
7. Aydog E, Ozturk G, Comert A, Tasdelen N, Akin O, Kulcu DG (2019) Sacroiliitis during isotretinoin treatment: causal association or coincidence? North Clin Istanb 6(1):75–80
8. Dawoud NM, Elnady BM, Elkhouly T, Yosef A (2018) Adalimumab as a successful treatment for acne fulminans and bilateral acute sacroiliitis with hip synovitis complicating isotretinoin therapy. Indian J Dermatol Venereol Leprol 84(1):104–107
9. Kocak O, Kocak AY, Sanal B, Kulan G (2017) Bilateral sacroiliitis confirmed with magnetic resonance imaging during isotretinoin treatment: assessment of 11 patients and a review of the literature. Acta Dermatovenerol Croat 25(3):228–233
10. Yildizgören MTET, Karatas Togral AA (2007) Bilateral sacroiliitis induced by systemic isotretionin treatment. West Indian Med J 66(1):187
11. Rodriguez-Lomba E, Molina-Lopez I, Monteagudo-Saez I, Suarez-Fernandez R, Campos-Dominguez M (2016) A case of acne fulminans with sacroiliitis successfully treated with methotrexate and isotretinoin. Dermatol Ther 29(6):476–478
12. Alkan S, Kayiran N, Zengin O, Kalem A, Kimyon G, Kilinc EO, Pehlivan Y, Kirtak N, Onat AM, Kisacik B (2015) Isotretinoin-induced spondyloarthropathy-related symptoms: a prospective study. J Rheumatol 42(11):2106–2109
13. Yilmaz Tasdelen O, Yurdakul FG, Duran S, Bodur H (2015) Isotretinoin-induced arthritis mimicking both rheumatoid arthritis and axial spondyloarthritis. Int J Rheum Dis 18(4):466–469
14. Cakir TSV, Bilgili A, Demirdal US, Ulker RN (2014) A case with bilateral sacroiliitis and polyneuropathy development due to isotretinoin use. Arch Rheumatol 29(4):304–308
15. Geller AS, Alagia RF (2013) Sacroiliitis after use of oral isotretinoin–association with acne fulminans or adverse effect? An Bras Dermatol 88(6 Suppl 1):193–196
16. Yilmazer B, Cosan F, Cefle A (2013) Bilateral acute sacroiliitis due to isotretinoin therapy: a case report. Int J Rheum Dis 16(5):604–605
17. Levinson M, Gibson A, Stephenson G (2012) Sacroiliitis secondary to isotretinoin. Australas J Dermatol 53(4):298–300
18. Zanelato TP, Gontijo GM, Alves CA, Pinto JC, Cunha PR (2011) Disabling acne fulminans. An Bras Dermatol 86(4 Suppl 1):S9–12
19. Barbareschi M, Paresce E, Chiaratti A, Ferla Lodigiani A, Clerici G, Greppi F (2010) Unilateral sacroiliitis associated with systemic isotretinoin treatment. Int J Dermatol 49(3):331–333. https://doi.org/10.1111/j.1365-4632.2009.04334.x
20. Rozin AP, Kagna O, Shiller Y (2010) Sacroiliitis and severe disability due to isotretinoin therapy. Rheumatol Int 30(7):985–986. https://doi.org/10.1007/s00296-009-1014-4
21. Gultepe M, Ozcan O, Ipcioglu OM, Kiralp MZ, Ozcakar L (2010) Sacroiliitis and muscle cramps in a healthy young man: some spearhead on MTHFR mutations. Rheumatol Int 30(7):995–996
22. Eksioglu E, Oztekin F, Unlu E, Cakci A, Keyik B, Karadavut IK (2008) Sacroiliitis and polyneuropathy during isotretinoin treatment. Clin Exp Dermatol 33(2):122–124
23. Dincer UCE, Kirat MZ, Dursun H (2008) Can isotretinoin induce sacroiliitis: three cases. Romatizma 23:157–159
24. Atabek MEPO, Elmas S (2007) Bilateral sacroiliitis following isotretinoin treatment in an adolescent with klinefelter syndrome. Endocrinologist 17:244–245
25. Bachmeyer C, Charoud A, Turc Y, Callot V, Blum L, Aractingi S (2003) Isotretinoin-induced bilateral sacroiliitis. Dermatology 206(3):285–286
26. Elias LM, Gomez MI, Torrelo A, Boixeda JP, Ledo A (1991) Acne fulminans and bilateral seronegative sacroiliitis triggered by isotretinoin. J Dermatol 18(6):366–367
27. Gasparyan AY, Ayvazyan L, Blackmore H, Kitas GD (2011) Writing a narrative biomedical review: considerations for authors, peer reviewers, and editors. Rheumatol Int 31(11):1409–1417
28. Sameem F, Semira (2016) Isotretinoin-induced acute severe myopathy involving pelvic girdle muscles: a case report. Indian J Pharmacol 48(5):601–603
29. Matsuoka LY, Wortsman J, Pepper JJ (1984) Acute arthritis during isotretinoin treatment for acne. Arch Intern Med 144(9):1870–1871
30. Pedraz T, Martinez A, Pascual E (2006) Acute hip monoarthritis in a patient treated with isotretinoin. J Clin Rheumatol 12(2):105–106
31. Hughes RA (1993) Arthritis precipitated by isotretinoin treatment for acne vulgaris. J Rheumatol 20(7):1241–1242
32. De Francesco V, Stinco G, Campanella M (1997) Acute arthritis during isotretinoin treatment for acne conglobata. Dermatology 194(2):195
33. Scheinfeld N, Bangalore S (2006) Facial edema induced by isotretinoin use: a case and a review of the side effects of isotretinoin. J Drugs Dermatol 5(5):467–468
34. Bergler-Czop B, Brzezinska-Wcislo L (2014) Pro-inflammatory cytokines in patients with various kinds of acne treated with isotretinoin. Postepy Dermatol Alergol 31(1):21–28
35. Frew JW, Hawkes JE, Krueger JG (2018) A systematic review and critical evaluation of immunohistochemical associations in hidradenitis suppurativa. F1000Res 7:1923
36. Bidad K, Salehi E, Jamshidi A, Saboor-Yaraghi AA, Oraei M, Meysamie A, Mahmoudi M, Nicknam MH (2013) Effect of all-transretinoic acid on Th17 and T regulatory cell subsets in patients with ankylosing spondylitis. J Rheumatol 40(4):476–483
37. Dalmolin RJ, Zanotto-Filho A, De Oliveira RB, Duarte RF, Pasquali MA, Moreira JC (2007) Retinol and retinoic acid increase MMP-2 activity by different pathways in cultured sertoli cells. Free Radic Res 41(12):1338–1347
38. Burrage PS, Mix KS, Brinckerhoff CE (2006) Matrix metalloproteinases: role in arthritis. Front Biosci 11:529–543
39. Slobodin G, Rimar D, Boulman N, Kaly L, Rozenbaum M, Rosner I, Odeh M (2016) Acute sacroiliitis. Clin Rheumatol 35(4):851–856
40. Firinu D, Garcia-Larsen V, Manconi PE, Del Giacco SR (2016) SAPHO syndrome: current developments and approaches to clinical treatment. Curr Rheumatol Rep 18(6):35
41. Pehlivan Y, Kisacik B, Sayiner ZA, Onat AM (2011) Inflammatory back pain in patients treated with isotretinoin. J Rheumatol 38(12):2690

42. Kamp S, Fiehn AM, Stenderup K, Rosada C, Pakkenberg B, Kemp K, Dam TN, Jemec GB (2011) Hidradenitis suppurativa: a disease of the absent sebaceous gland? Sebaceous gland number and volume are significantly reduced in uninvolved hair follicles from patients with hidradenitis suppurativa. Br J Dermatol 164(5):1017–1022
43. Gallagher CG, Kirthi SK, Cotter CC, Revuz JR, Tobin AMT (2019) Could isotretinoin flare hidradenitis suppurativa? A case series. Clin Exp Dermatol. https://doi.org/10.1111/ced.13944
44. De Souza A, Solomon GE, Strober BE (2011) SAPHO syndrome associated with hidradenitis suppurativa successfully treated with infliximab and methotrexate. Bull NYU Hosp Jt Dis 69(2):185–187
45. Leybishkis B, Fasseas P, Ryan KF, Roy R (2001) Hidradenitis suppurativa and acne conglobata associated with spondyloarthropathy. Am J Med Sci 321(3):195–197
46. Marquardt AL, Hackshaw KV (2009) Reactive arthritis associated with hidradenitis suppurativa. J Natl Med Assoc 101(4):367–369
47. Fioravanti A, Lauraflori M, Guidelli GM, Giordano N (2011) Dactylitis as a first manifestation of arthritis associated with hidradenitis suppurativa. Indian J Dermatol Venereol Leprol 77(1):74–76