

Relapsing polychondritis with pituitary adenoma

Hipofiz adenomu ile tekrarlayan polikondrit birlikteliği

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Abstract

Relapsing polychondritis (RP) is an autoimmune disease with unknown etiology, and mainly affects cartilaginous and non-cartilaginous organs. The RP is also associated with some solid tumors such as lung cancer, Kaposi sarcoma, and prostate cancer. There is no single effective treatment for alleviating symptoms or prevention of disease progression. However, corticosteroids are the main choices of RP treatment. The other drugs included immunosuppressive agents. Here, we present a new case of a patient who was diagnosed with relapsing RP along with pituitary adenoma and showed the effectiveness of etanercept [anti-tumor necrosis factor (TNF) agent] in the control with arthritis. Pituitary adenoma can develop following relapsing RP and should therefore be considered in the RP diagnostic procedure, and it could be affected on the patient's visual field test. Also, immunosuppressive agents such as anti-TNF agents can be used to control the disease.

Keywords: Relapsing polychondritis, cancer-related polychondritis, polychondritis, pituitary adenoma, anti-TNF

Öz

Tekrarlayan polikondrit (TP), etiyojisi bilinmeyen ve esas olarak kırıkırdaklı ve kırıkırdaksız organları etkileyen otoimmün bir hastalıktır. RP ayrıca akciğer kanseri, Kaposi sarkomu ve prostat kanseri gibi bazı solid tümörlerle de ilişkilidir. Semptomları hafifletmek veya hastalığın ilerlemesini önlemek için tek bir etkili tedavi yoktur. Bununla birlikte, kortikosteroidler TP tedavisinin ana seçimidir. Diğer ilaçlar, immünoşüpresif ajanları içerir. Burada, hipofiz adenomu ile birlikte tekrarlayan RP tanısı alan ve artrit kontrolünde etanerseptin [anti-tümör nekroz faktör (TNF) ajan] etkinliğini gösteren yeni bir olguyu sunduk. Hipofiz adenomu nükseden TP sonrası gelişebilir ve bu nedenle RP tanı prosedüründe düşünülmelidir ve hastanın görme alanı testinden etkilenebilir. Ayrıca hastalığı kontrol altına almak için anti-TNF ajanları gibi immünoşüpresif ajanlar kullanılabilir.

Anahtar Kelimeler: Tekrarlayan polikondrit, kansere bağlı polikondrit, polikondrit, hipofiz adenomu, anti-TNF

Introduction

Relapsing polychondritis (RP) is a rare autoimmune disease with unclarified etiology, mainly affecting the cartilaginous tissues of the body. Nevertheless, other non-cartilaginous and proteoglycan rich tissues may also be affected. RP is a relatively rare disease without an animal model, making it more difficult to assess the pathophysiology of the disease. RP is a life-threatening disease because it is often difficult to diagnose and treat.^[1] The disease is a heterogeneous phenotype with different episodes and progressive.^[2] The most common clinical presentations of RP are seronegative arthritis, laryngotracheal symptoms,

nasal chondritis, ocular inflammation, and auricular chondritis.^[1,3] Additionally, respiratory problems, infection, and cardiac complications with valvular involvement are the most common causes of morbidity and mortality in RP patients.^[1]

Less commonly, RPs also associated with some benign and malignant solid tumors. Cancer-related RPs are reported, including lung cancer,^[4,5] Kaposi sarcoma,^[6] prostate cancer, malignant fibrous histiocytoma, soft-tissue sarcoma, breast cancer, urothelial carcinoma, and vocal cord tumor (glottis).^[4,7]

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There is no uniformly effective treatment for alleviating symptoms or the prevention of disease progression. Meanwhile, corticosteroids are the main choice of RP treatment.^[4] Other treatment strategies are dapsone, non-steroidal anti-inflammatory drugs, and colchicine, which have been proposed for mild RP patients.^[7,8] Immunosuppressive agents, such as mycophenolate mofetil, cyclosporine, azathioprine, cyclophosphamide,^[7] and anti-tumor necrosis factor (anti-TNF),^[9] have also been applied to patients with severe symptoms of refractory or relapsing RP cases. The current study presented a new case of a patient diagnosed with RP along with pituitary adenoma and showed the effectiveness of etanercept (an anti-TNF agent) in control with refractory arthritis.

Case Report

A 52-year-old Iranian woman who presented with a 10-year history of joint pain and recurrent attacks of episcleritis was referred to the rheumatology clinic due to pain and swelling in the joints of the hands and wrists. Based on the patient's medical history, she had controlled mild hypertension with losartan tablets (25 mg/day) and due to the red retina has been examined several times by an ophthalmologist. She had complained of recurrent attacks of earlobe redness recurring every two to three months at the same time with the redness of the eye and was accompanied by pain and swelling of the earlobe.

On examination, she had arthritis of the right wrist and metacarpophalangeal 2 and 3 in both hands and other joints were normal. In complete ENT examination (inspection of the face, ears, nose, throat, and neck), only chondritis of the earlobe was observed (Figure 1). The only abnormal laboratory findings (Table 1) were high C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR).

Due to recurrent attacks of chondritis, episcleritis, and arthritis with relapsing polychondritis diagnosis, she was treated with prednisolone (5 mg/day) and methotrexate (10 mg/weekly). The symptoms of arthritis completely improved and recurrent attacks of the eyes and earlobes were not repeated. ESR was reduced from 43 to 12 mm/hour. After eight months of treatment, she again complained of arthritis attacks in the joints of the shoulders, knees, and ankles. Therefore, the doses of prednisolone and methotrexate were increased (50 mg/day and 20 mg/weekly, respectively). After reducing the dose of prednisolone, the symptoms recurred and the severity of symptoms and pain led to her hospitalization. The patient's ESR increased from 12 to 80 during a recent relapse. Malignancy was assessed due to the association of recurrent polychondritis with some tumors.



Figure 1. An ENT examination was observed chondritis of the earlobe

Table 1. Laboratory findings

Laboratory test	Results	
White blood cells (WBC)	8700	
Red blood cell (RBC)	4100000	
Hemoglobin (Hb)	12 g/dL	
Hematology	Hematocrit (HCT)	39
	Mean corpuscular volume (MCV)	81
	Mean corpuscular hemoglobin (MCH)	29
	Mean corpuscular hemoglobin concentration (MCHC)	32
	Platelet (Plt)	326×10 ³ /mL
	Erythrocyte sedimentation rate (ESR)	43 mm/hour *
	C-reactive protein (CRP)	32.0 mg/L *
Serology	Anti-cyclic citrullinated peptide antibody (anti-CCP)	Negative
	Anti-neutrophil cytoplasmic antibodies (ANCA)	Negative
	Rheumatoid factor (RF)	Negative
	ANA (anti-nuclear antibody)	Negative
Biochemistry	AST	17
	ALT	23
	BUN	0.9
	Urine analysis (UA)	Normal
Microbiology	Tuberculin test for tuberculosis (PPD)	Negative
	HBV markers	Negative
	HCV antibodies	Negative
	Brucellosis antibodies	Negative
	Chest X-rays (for ruled out tuberculosis)	Normal

* Abnormal range

CT scans of the lungs, abdomen, pelvis, ear, throat, and nose were normal. Digital mammography was normal.

Following relapsing RP, the patient was treated with subcutaneous etanercept (50 mg/weekly), prednisolone (15 mg/day), and methotrexate (20 mg/weekly). The patient's symptoms significantly improved and the pain was controlled. The ESR was reduced to 23 after two months, during which the dose of prednisolone was reduced to 5 mg/day. In the third month of etanercept therapy, the patient complained of headaches and laboratory tests demonstrated a slight increase in prolactin and the visual field test showed temporal hemianopia (Figure 2). Magnetic resonance imaging of the pituitary gland and Sella turcica revealed the enhancing intrasellar mass with extended to supraspace containing high signal area on T1 weighted (hemorrhage) and cystic change, which was suggested to be pituitary macroadenoma with a compression effect on optic chiasma and displacement of pituitary infundibulum (Figure 3). The patient underwent surgery and pathological examinations confirmed non-functioning pituitary adenoma (Figure

4). The patient's headache and visual field test improved following surgery. Finally, the treatment was continued with prednisolone (5 mg/day), methotrexate (15 mg/weekly), and etanercept subcutaneously (50 mg/week).

Discussion and Conclusion

Relapsing polychondritis (RP) is a rare recurrent auto-inflammatory disorder attacking cartilage and non-cartilage tissues, particularly the ear, nose, and tracheobronchial. The diagnosis of RP is commonly based on clinical features without specific serologic tests.^[1] RP diagnosis is according to McAdams's criteria and three of the six following signs are essential: Audio-vestibular damage, respiratory tract chondritis, ocular inflammation, nasal chondritis, non-erosive seronegative inflammatory arthritis, and bilateral auricular chondritis. Damiani and Levine modified McAdams's criteria as following: McAdam criteria along with patient's response to corticosteroids or having McAdam criteria with tissue diagnosis.^[7] Another criterion for RP diagnosis is the Michet criteria, including

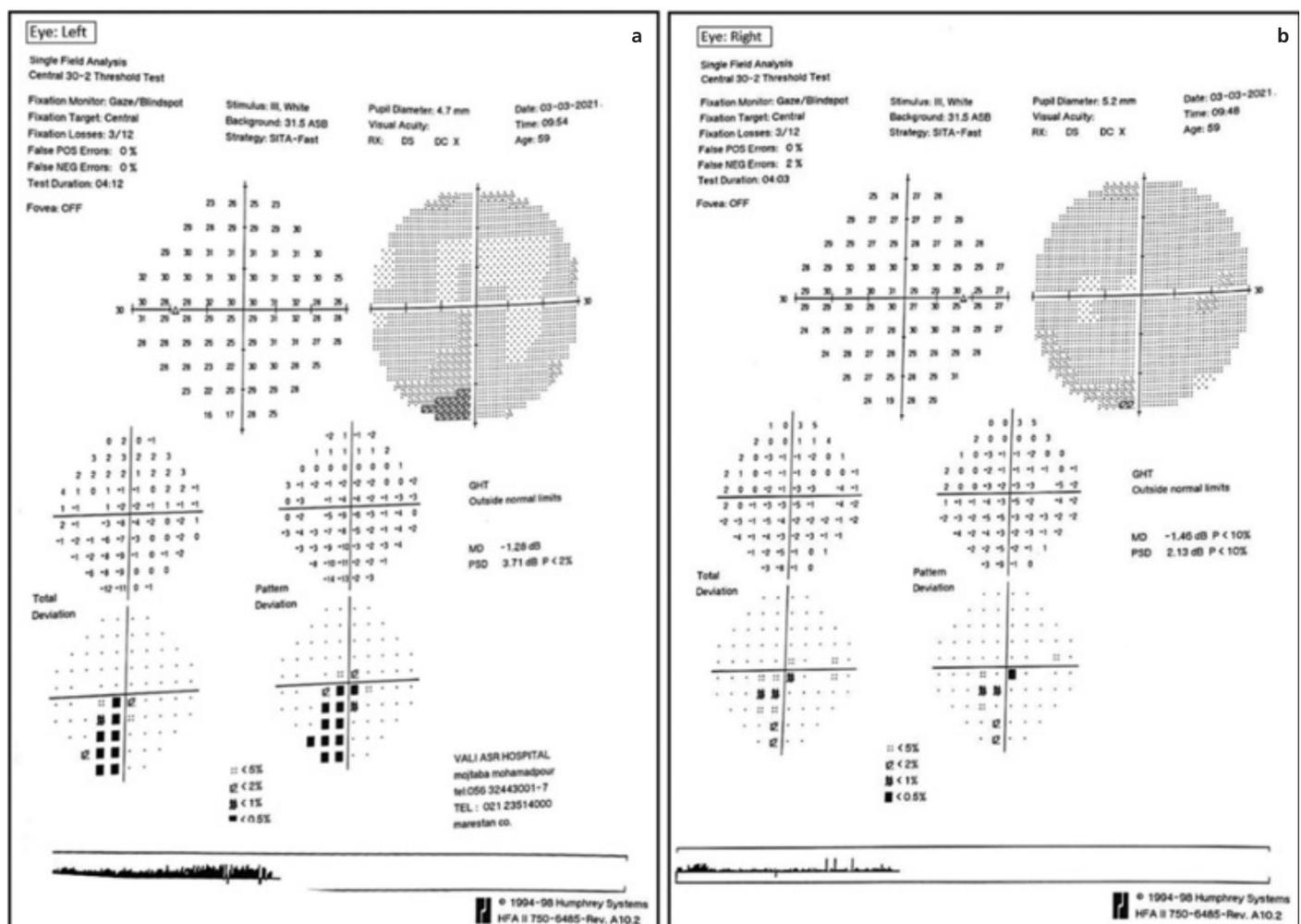


Figure 2a. The visual field test showed temporal hemianopia in left eye, **b.** and right eye

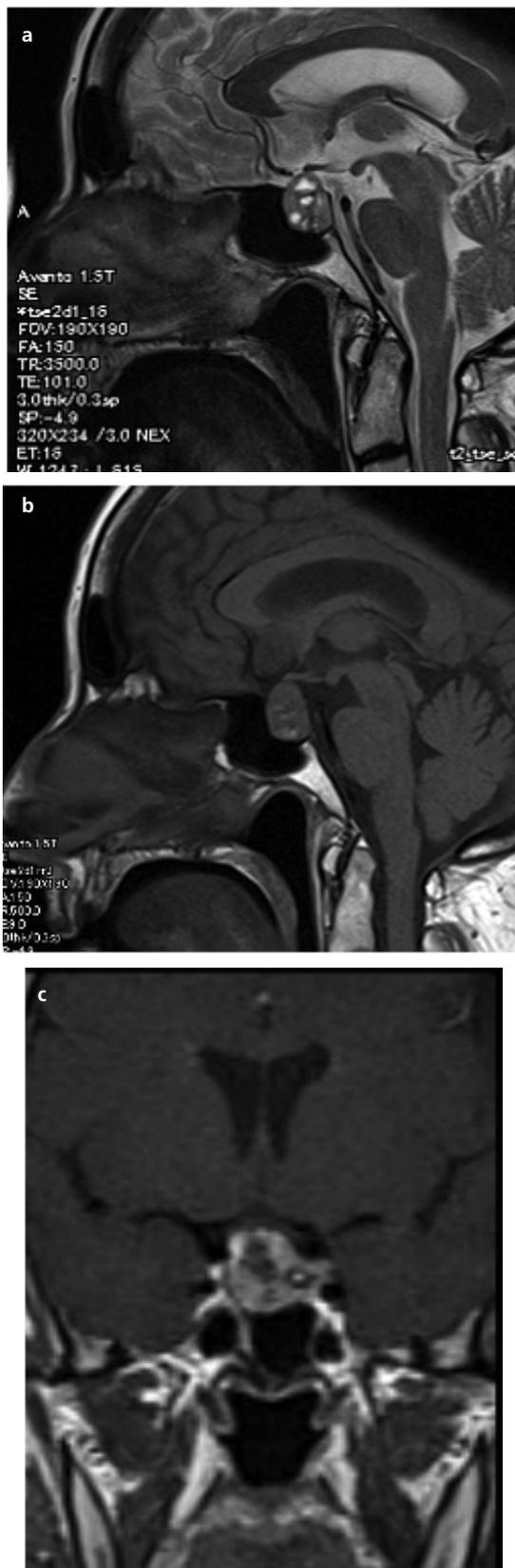


Figure 3. MRI of the pituitary gland and Sella turcica showed the enhancing intrasellar mass with extension to supra space (23×12×16 mm) containing high signal area on T1 weighted (a & b) hemorrhage and cystic change. c) pituitary macroadenoma with compression effect on optic chiasma

MRI: Magnetic resonance imaging

proven inflammation in two of the three parts of the body (laryngotracheal cartilages, nasal, and auricular) along with two manifestations, namely, hearing loss, seronegative arthritis, vestibular dysfunction, and ocular inflammation.^[1] Here, our patient had recurrent chondritis, episcleritis, and arthritis with the diagnostic criteria of Michet in the absence of evidence of another disease.

In RP disease, the laboratory findings could be indicative of inflammation or sometimes tissue damage, urinalysis, and liver function tests are useful to detecting renal and liver function disorders, respectively.^[7] Other laboratory tests, such as anti-phospholipid antibodies, anti-nuclear antibody, rheumatoid factor, and complement serum levels, could be helpful to diagnose RP or prove the presence of concurrent diseases.^[10] In our patient, increased CRP and ESR were observed and other tests were negative.

Several studies have shown a significant association of RP with some malignancies and RP and cancer could occur at the same time. For example, myelodysplastic syndrome (MDS) has been reported in correlation with RP and it can occur after, simultaneously, with/or before RP, and in patients with MDS with RP, mortality is high.^[11-13] In a study by Francès et al.,^[14] on 200 patients with RP, the MDS was diagnosed in 22 cases. In this regard, with several published cases occurring in males' patients, also there may be strong sex priority. Also, Hodgkin and non-Hodgkin have been described in RP patients.^[13,15,16] Although, there is a high association with a large number of patients with both diseases, its basis is unknown. In a study by Tomomatsu et al.,^[17] a patient with simultaneously MDS and RP has reported following a transplantation of non-myeloablative allogeneic bone marrow from a sibling donor, suggesting that the RP in this case may have been a paraneoplastic complication of the hematologic disorder. In several reports, the diagnosis of malignancies often occurred after RP in 10 cases with active disease (mean duration of 30 months).^[4] Less commonly, RP is also associated with some benign and malignant solid tumors. The association of colorectal cancer with RP is rather uncommon and has been detected in three RP patients.^[7] In a study by Gning et al.,^[18] a 30-year-old female patient was reported with rectal cancer with RP and no special associated features were recorded. Lung cancer has also been reported in three RP patients.^[5] Other tumors reported include vocal cords tumor (glottis), Kaposi sarcoma,^[6] breast cancer, prostate, soft-tissue sarcoma, urothelial carcinoma, and malignant fibrous histiocytoma.^[4,7] Additionally, cutaneous features and the variety of skin lesions are reported in cancer-related RP, such as pyoderma gangrenosum, dermatomyositis, and musculo-aponeurotic fibromatosis.^[4] Hence, cutaneous-related RP could be a

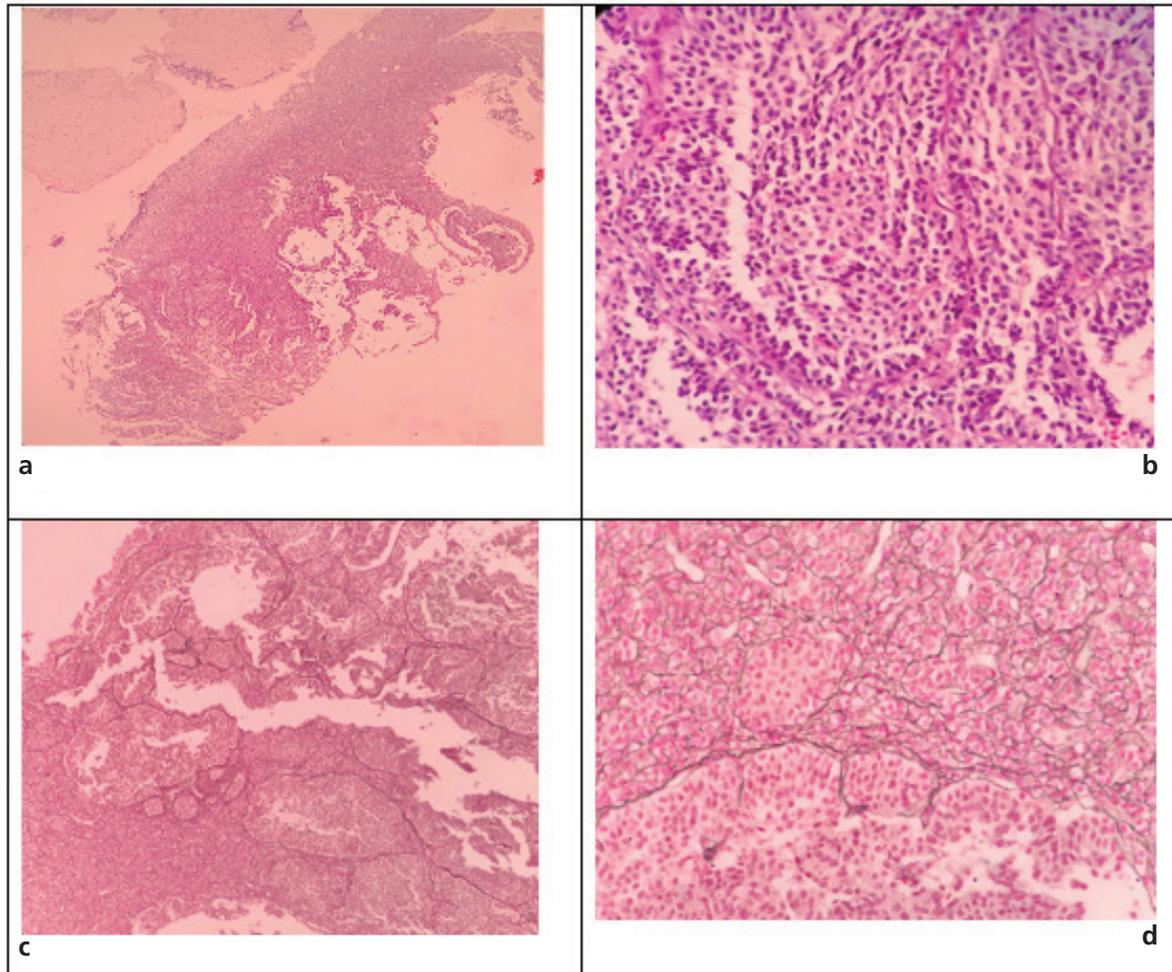


Figure 4. Histopathological image of non-functioning pituitary adenoma. **a & b.** Proliferation of monomorphous cells with round nuclei and vesicular chromatin and acidophilic cytoplasm (Hematoxylin & eosin stain), **c & d.** Reticulin-specific staining: Lack of usual acinar design

potential predictor of further cancer in RP cases. In our patient, detected pituitary adenoma was observed after several temporary remissions were presented without any cutaneous manifestation. A pituitary adenoma is usually associated with increased prolactin levels. In a study by Ahmed et al.,^[19] five cases of pituitary adenoma with elevated PRL levels were reported and in this regard, our case also demonstrated an increase in prolactin levels.

No uniformly effective treatments for alleviating symptoms or the prevention of disease progression exist yet. Studies have shown that RP is mostly treated with corticosteroids, such as prednisolone.^[4] Immunosuppressive agents, such as cyclosporine A, methotrexate, azathioprine, and cyclophosphamide also approved for patients with severe symptoms of refractory or relapsing RP.^[4,7] In 2010 a study reported an RP therapy with TNF- α -antagonists, such as etanercept, resulting in a significant alleviate disease activity. In our case, the patient's symptoms significantly improved

with subcutaneous etanercept (50 mg/weekly), prednisolone (15 mg/day), and methotrexate (20 mg/weekly). These results may alter the part of immunosuppressive therapy in RP pathogenesis.^[20]

Pituitary adenoma can develop following relapsing RP and should therefore be considered in RP diagnostic procedure and it could affect the patient's visual field test. Additionally, immunosuppressive agents, such as anti-TNF agents, can be used to control the disease. It is also suggested that RP patients should be followed up for tumors thorough physical examination, radiological and laboratory investigations, physical examination, and history. RP patients should also be screened more carefully even in the remission of disease for early detection of tumors.

Ethic

Informed Consent: This case report was presented to the ethics committee of Birjand University of Medical

Sciences and approved with the following code: IR.BUMS.REC.1400.123. Written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: N.N., Z.S., Design: Z.S., Data Collection or Processing: Z.S., Analysis or Interpretation: Z.S., Literature Search: Z.S., Writing: N.N., Z.S.

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