

# Multiple Conjunctival Lesions in a Patient with Polyarteritis Nodosa and Familial Mediterranean Fever

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*This report is of an 18-year-old man with familial Mediterranean fever and polyarteritis nodosa with multiple subconjunctival nodular lesions in both eyes. Detailed ophthalmological examination showed bilateral multiple conjunctival nodular lesions. Histopathological examination revealed adipocytes, increased congested vascular structures, and plasma cell infiltration in fibrous tissue samples; a benign atypical lipoid tumour was diagnosed. Open angle glaucoma was also present. Various ocular pathologies, including episcleritis, anterior uveitis, panuveitis, retinal tear, and rhegmatogenous retinal detachment have been reported in association with familial Mediterranean fever. The unique feature of this patient was the unusual coexistence of familial Mediterranean fever and polyarteritis nodosa with bilateral conjunctival atypical lipoid tumours and glaucoma.*

**Key words:** Conjunctival neoplasms, Familial Mediterranean fever, Glaucoma, Polyarteritis nodosa

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## Introduction

Familial Mediterranean fever (FMF) is caused by mutations in the gene encoding pyrin and is characterised by self-limiting recurrent attacks of fever, peritonitis, pleuritis, arthritis, and erysipelas-like erythema.<sup>1-7</sup> Pyrin protein interacts with other proteins involved in inflammation and apoptosis, and can cause renal failure by amyloidosis if left untreated.<sup>1-7</sup> Some vasculitic diseases, including polyarteritis nodosa (PAN), Henoch Schonlein purpura, and Behçet's disease can coexist with FMF.<sup>1-3</sup> PAN is a vasculitis of the small- and medium-sized arteries, and is characterised by immune complex deposition, inflammation, and necrosis of the intimal and medial layers of vessel walls.<sup>1-3</sup> Skin vasculitis, myalgia, peripheral neuropathy, hypertension, and renal, central nervous system, and gastrointestinal system involvement are frequently seen. Approximately 0.8% of individuals with FMF have PAN.

Various ocular pathologies such as uveitis, episcleritis, and retinal changes have been reported in patients with FMF.<sup>3-7</sup> These conditions may be due to inflammation associated with FMF. However, to the authors' knowledge, there have been no previous reports of ocular findings in patients with coexisting FMF and PAN.

This report is of a patient with FMF and PAN with previously unreported ocular findings.

## Case Report

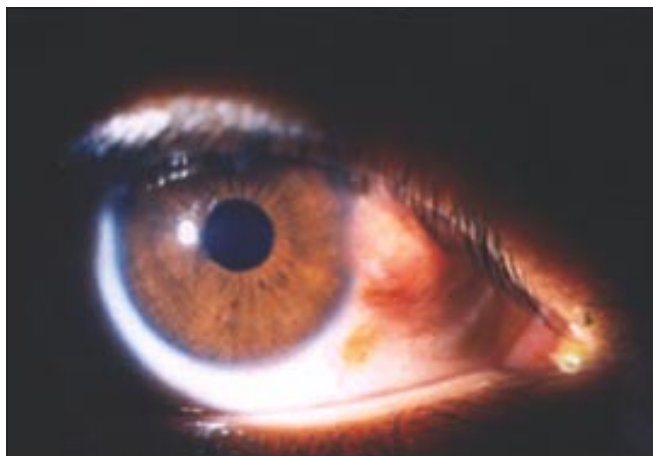
An 18-year-old man with FMF and PAN was referred to the Ankara Ulucanlar Eye Research Hospital, Ankara, Turkey, in May 2004 for redness and multiple conjunctival nodular lesions in both eyes for the previous 3 years. He had no pain or irritation.

According to his medical history, he had had recurrent short attacks of fever and abdominal pain at the age of 6 years. On the basis of the clinical findings and a favourable response to colchicine treatment, FMF was diagnosed. At the age of 12 years, he had weakness, malaise, and severe myalgia in addition to abdominal pain, and a diagnosis of PAN was made according to the muscle biopsy, which showed infiltration of vessels and perivascular areas by polymorphonuclear neutrophils and intimal proliferation. He had been treated with long-term prednisolone 0.5 to 1 mg/kg/day for 4 years. Corticosteroid therapy had been tapered and stopped twice, but was restarted due to severe relapse. The patient had had annual ophthalmological examinations during this time, but no ocular pathologies were detected, except for conjunctival lesions at the age of 15 years. Aseptic femur necrosis occurred at the age of 16 years and corticosteroid therapy was discontinued. Colchicine 1.0 mg twice daily and cyclosporine 100 mg/day were started and

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## Conjunctival Lesions in Polyarteritis Nodosa and Familial Mediterranean Fever

Figure 1. Slit-lamp appearance of the largest conjunctival nodular lesion.

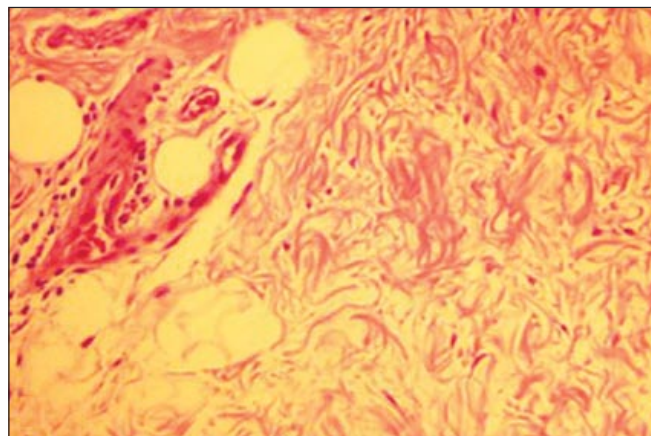


the systemic symptoms of both diseases have been controlled. He has had no renal involvement.

At presentation to the Ankara Ulucanlar Eye Research Hospital, his best-corrected visual acuity was 20/20 in both eyes. Slit-lamp biomicroscopic examination revealed bilateral multiple conjunctival nodular lesions adherent to the conjunctival and scleral tissues (Figure 1). The intraocular pressure (IOP) was measured twice daily for 3 days with a Goldmann applanation tonometer and the mean IOP was 23 mm Hg in the right eye and 24 mm Hg in the left eye. Fundus examination with a 90 D lens revealed a cup-disc ratio of 0.6. There were large pores on the lamina cribrosa and notches at the inferior and superior part of the disc. There were bends in the retinal vessels as they shifted from a vertical orientation along the cup wall to a horizontal orientation on the retinal surface in both eyes. Perimetric examination showed enlargement of the blind spot and an absolute arcuate scotoma, involving the entire superonasal and half of the superotemporal quadrant, in the right eye, with a mean deviation (MD) of -12.1. Enlargement of the blind spot, generalised depression, and temporal wedge with a MD of -10.4 were detected in the left eye. Gonioscopic examination showed grade 4 open angles in both eyes. He was diagnosed with steroid-induced open angle glaucoma, and topical brimonidine twice daily was administered. After the first week of treatment, the IOP was reduced to 16 mm Hg in the right eye and 15 mm Hg in the left eye.

Incisional biopsies were performed under topical lidocaine anaesthesia to diagnose the conjunctival nodular lesions. The samples were stained with dye. Light microscopy examination of the haematoxylin and eosin-stained sections revealed adipocytes with increased congested vascular structures and plasma cell infiltration in fibrous tissue samples (Figure 2). There were no morphological signs of either vasculitis or amyloid. Atypical lipoid tumour was diagnosed based on these findings.

Figure 2. Histological section of the lesion showing adipocytes, increase in congested vascular structures, and plasma cell infiltration (haematoxylin and eosin; original magnification, x 10).



The patient was followed up for approximately 20 months. The IOP remained controlled and there was no worsening of visual field defects and glaucomatous optic nerve damage during the follow-up period. Pain and irritation and enlargement of the conjunctival nodular lesions were not observed.

### Discussion

FMF is characterised by self-limiting recurrent attacks of fever and serositis and is caused by mutations in the pyrin gene.<sup>1-7</sup> The coexistence of this condition with PAN has been increasingly reported.<sup>1-3</sup> Various ocular pathologies, including episcleritis, anterior uveitis, panuveitis, retinal tear, and rhegmatogenous retinal detachment have been reported in FMF.<sup>3-7</sup>

Scharf et al reported episcleritis in 2 adults with FMF<sup>4</sup> and Yazici and Pazarli described episcleritis and anterior uveitis in a 28-year-old woman with FMF.<sup>5</sup> Panuveitis and episcleritis have been reported in siblings with FMF aged 7 and 11 years.<sup>6</sup> Recurrent bilateral panuveitis and rhegmatogenous retinal detachment have been reported in a 19-year-old patient with FMF.<sup>7</sup>

To the author's knowledge, there have been no previous reports of ocular findings in patients with coexisting FMF and PAN. This patient had multiple bilateral conjunctival nodular lesions, which were diagnosed as atypical conjunctival benign lipoid tumour, with congested vascular structures and plasma cell infiltration into fibrous tissue samples. No amyloid material or vasculitis were found in the conjunctival lesions so it is likely that the conjunctival lesions were not part of the pathology of FMF and PAN.

This patient also had open angle glaucoma. The most likely cause of glaucoma was thought to be the long-term use of corticosteroids. He had used systemic corticosteroid for approximately 4 years until treatment was discontinued because of aseptic femur necrosis. He was then treated with colchicine and cyclosporine for

the previous 2 years. Another probable mechanism of his glaucoma was thought to be the blockage of trabecular outflow by amyloid material present in the tissues of patients with FMF. Future histopathological examination of the trabecular tissue is planned if trabeculectomy becomes necessary. It was also thought that a decrease in uveoscleral outflow due to the multiple conjunctival nodular lesions adherent to conjunctival and scleral tissues may be a cause of glaucoma. However, this patient may have had juvenile glaucoma, independently of FMF and PAN.

The unique feature of this patient was the unusual coexistence of FMF and PAN with conjunctival nodular lesions and glaucoma. This report emphasises the importance of detailed ophthalmological examination of patients with FMF and systemic vasculitic disorders for early diagnosis of glaucoma to prevent optic nerve damage.

## **References**

1. Glikson M, Galun E, Schlesinger M, et al. Polyarteritis nodosa and familial Mediterranean fever: a report of 2 cases and review of the literature. *J Rheumatol.* 1989;16:536-9.
2. Ozen S, Ben-Chetrit E, Bakkaloglu A, et al. Polyarteritis nodosa with familial Mediterranean fever (FMF): a concomitant disease or a feature of FMF? *Semin Arth Rheum.* 2001;30:281-7.
3. Oguzkurt P, Akcoren Z, Kale G, Tanyel C. Polyarteritis nodosa involving the hepatobiliary system in an eight-year-old girl with a previous diagnosis of familial Mediterranean fever. *Eur J Pediatr Surg.* 2000;10:145-7.
4. Scharf J, Meyer E, Zonis S. Episcleritis associated with familial Mediterranean fever. *Am J Ophthalmol.* 1985;100:337-9.
5. Yazici H, Pazarli H. Eye involvement in a patient with familial Mediterranean fever. *J Rheumatol.* 1982;9:644.
6. Akman A, Varan B, Akova Y, Aydin P. Ocular involvement in siblings with familial Mediterranean fever. *J Pediatr Ophthalmol Strabismus.* 2001;38:114-6.
7. Hirsh A, Huna R, Ashkenazi I, Bartov E, Blumenthal M. Recurrent bilateral panuveitis and rhegmatogenous retinal detachment in a patient with familial Mediterranean fever. *Am J Ophthalmol.* 1990;110:702-3.