Case Report

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Effects of surgery and topical medication on eosinophilic granulomatosis with polyangiitis with otitis media and sinusitis: a case report

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Abstract

Eosinophilic granulomatosis with polyangiitis (EGPA), also known as Churg–Strauss syndrome, is eosinophil-rich, necrotizing granulomatous inflammation often involving the respiratory tract. Furthermore, EGPA is necrotizing vasculitis that predominantly affects small to medium vessels and is associated with asthma and eosinophilia. Most patients with EGPA have sinusitis and some complain of hearing loss and refractory otitis media with effusion. Systemic use of immunosuppressants and glucocorticoids is currently recommended, despite the inevitable associated side effects. However, systemic treatment is not always effective for nasal and ear symptoms. We report a case of EGPA with refractory otitis media and chronic sinusitis, which were resistant to systemic high-dose steroids and immunosuppressants. However, these symptoms responded well to functional endoscopic sinus surgery and myringotomy and grommet insertion. We also administered budesonide nasal irrigation and glucocorticoid injection by intratympanic and postaural methods in this patient. The therapeutic effect was satisfactory.

Keywords

Eosinophilic granulomatosis with polyangiitis, Churg–Strauss syndrome, otitis media, chronic sinusitis, nasal irrigation, glucocorticoid

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Introduction

Eosinophilic granulomatosis with polyangiitis (EGPA), also known as Churg–Strauss syndrome, is eosinophil-rich, necrotizing granulomatous inflammation often involving the

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respiratory tract. Furthermore, EGPA is necrotizing vasculitis that predominantly affects small to medium vessels and is associated with asthma and eosinophilia.[1,2] The prevalence of EGPA is 10.7 to 13/1,000,000.[3] EGPA is usually associated with respiratory problems, such as asthma and sinusitis, eosinophilia, neuropathy, pulmonary infiltrates, and vasculitis, and can also cause myocarditis and glomerulonephritis. Systemic use of immunosuppressants and glucocorticoids is currently recommended for this condition, despite the inevitable associated side effects.[4]

Most patients with EGPA have sinusitis and some complain of hearing loss and refractory otitis media with effusion.[5,6] We report a case of EGPA with refractory otitis media and chronic sinusitis, which were resistant to systemic high-dose steroids and immunosuppressants. However, these symptoms responded well to functional endoscopic sinus surgery, and myringotomy and grommet insertion. We also performed budesonide nasal irrigation and glucocorticoid injection by intratympanic and postaural methods in this patient.

Case report

A 45-year-old woman had suffered from asthma and rashes for 8 years (from 2011–2019). She also had eosinophilia (>10%), neuropathy, recurrent mucous rhinorrhea, and nasal obstruction. A skin biopsy showed eosinophilic leukocytoclastic vasculitis in vessels. Eosinophils were also observed in a gastric mucosal biopsy and bronchial perfusate. A test of the perinuclear pattern of antineutrophilic cytoplasmic autoantibodies was positive. She also had symptoms of stomach ache and acid reflux. A fecal occult blood test was positive. Gastroscopy showed active inflammation and lymphatic tissue hyperplasia of the gastric mucosa. The number of eosinophils was 20/HPF. However, there was no evidence of gastrointestinal perforation. Therefore, in 2012, she was diagnosed with Churg–Strauss syndrome according to American College of Rheumatology 1990 criteria.[7] She was then treated in the Rheumatology Department by administration of high-dose steroids and immunosuppressants for recurrent shortness of breath, lung infection, and pain in both lower limbs and intermittent numbness for approximately 7 years (from 2012–2019). She was provided therapy of cyclophosphamide with a dose of 750 mg every 3 weeks for eight cycles and prednisolone with a dose of 50 mg/day for 3 weeks, followed by gradual tapering to the minimal effective dose. The above-mentioned symptoms were recurring, but responded to the therapy. However, 3 years previously (in 2016), she began to develop nasal congestion, rhinorrhea, and aural fullness, and they were resistant to treatment from the Rheumatology Department of large doses of steroids and immunosuppressants for 6 months (methylprednisolone pulses 500 mg/day for 3 days and cyclophosphamide 750 mg every 2 weeks). To prevent serious side effects of cyclophosphamide, she was treated with mycophenolate mofetil instead of cyclophosphamide 1 year before surgery (in 2016) because the cumulative dose of cyclophosphamide was up to 35 g. Since then, she was treated with prednisolone 50 mg/day and mycophenolate mofetil 750 mg, twice a day during the exacerbation period of the disease as induction therapy. The use of antibiotics depended on the results of bacterial culture. The dose of prednisolone was tapered off (5 mg every 2 weeks) if the disease was well controlled. The maintenance dose was prednisolone 12.5 mg/day and mycophenolate mofetil 500 mg, twice a day. Because her asthma tended to occur at doses < 12.5 mg of prednisolone, she had to take medicine continuously. Additionally, the side effect of osteoporosis occurred during treatment, which also limited the use of systemic

steroids as a treatment for the symptoms of otolaryngology.

She visited our department to investigate recurrent rhinorrhea and bilateral hearing loss in 2017. Peripheral blood examinations showed a leukocyte count of 7400 mm^{-3} with 8.5% eosinophils at that time. Nasal endoscopy showed nasal polyps of the middle nasal meatus and a swollen pharyngeal orifice of the eustachian tube with mucus on both sides (Figure 1a, b, c). Otoscopy showed severe otitis media with effusion in both ears. Computed tomography (CT) imaging of the temporal bone showed a soft tissue shadow in the middle ear cavities, antrums, and mastoid cells. Pure tone audiometry showed conductive hearing loss in both ears. Nasal polyps and granulomatous lesions in the middle ear may reduce the effect of topical medication. Therefore, we thought that surgical treatment was necessary and the combination of topical medication after surgery might relieve her symptoms of otolaryngology.

We operated on the patient when the vasculitis was stable. The C-reaction protein level was 0.48 mg/L and blood sedimentation was 2 mm/hour before surgery. The maintenance dose was prednisolone 12.5 mg/day and mycophenolate mofetil 500 mg, twice a day. The asthma and lung infection were better controlled before surgery and her lung function met the standards of general anesthesia. Her coagulation function was also normal. We then performed endoscopic sinus surgery and ventilation tubes were inserted in both ears. Otitis media was treated with an injection of dexamethasone into the middle ear

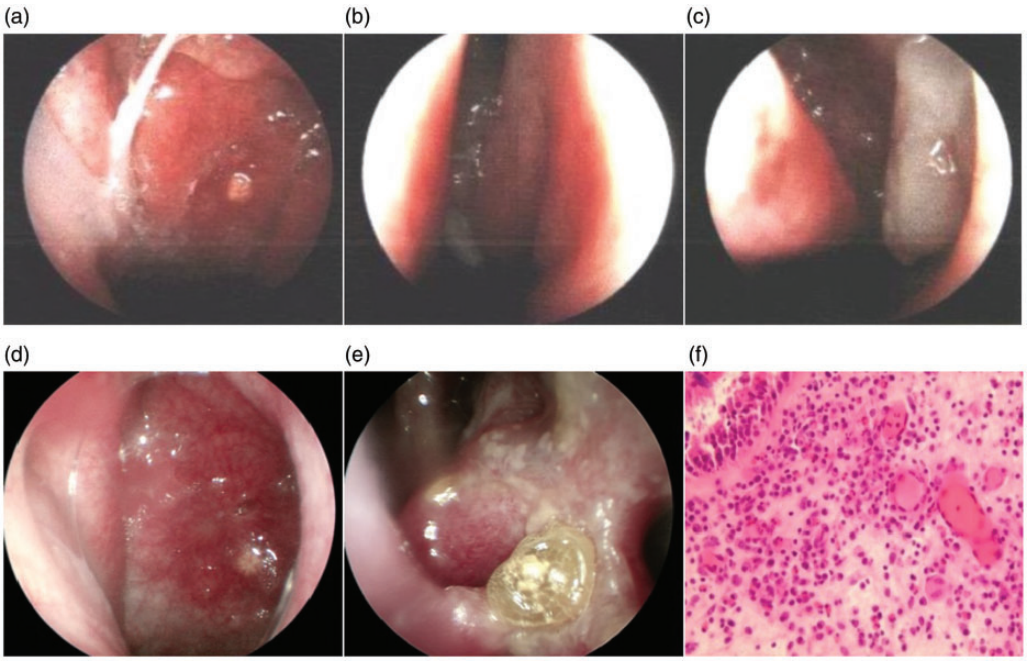

Figure 1. (a) A swollen pharyngeal orifice of the eustachian tube with mucus on the right side before surgery can be seen. (b, c) Polyps in the middle nasal meatus on the left side and in the olfactory cleft on the right side can be seen. (d) Swelling of the pharyngeal orifice of the eustachian tube had disappeared 4 months after surgery. (e) A few scabs in the nasal cavity were observed 4 months after surgery. (f) Histopathology shows eosinophilic infiltration of nasal polyps after surgery.

cavity through ventilation tubes in both ears. Treatment after surgery was budesonide nasal irrigation (one pack of 1 mg/2 mL budesonide respules mixed into a squeeze bottle with 250 mL normal saline). She recovered well after surgery and we advised her to visit the Rheumatology Department for reexamination regularly after discharge. Four months after surgery, she returned to our department because slight aural fullness on her left ear had reappeared after bilateral ventilation tubes were dislodged. We performed nasal endoscopy and found that swelling of the pharyngeal orifice of the eustachian tube had disappeared and that there were a few scabs in the nasal cavity (Figure 1d, e). Histopathology of nasal polyps showed eosinophilic infiltration (Figure 1f). Pure tone audiometry showed that her air–bone gap had decreased to normal. We treated her left ear with betamethasone (7 mg) injection by the postaural method. She was subsequently treated intermittently in the Rheumatology Department for pulmonary infection and wheezing, and no serious otolaryngological symptoms have recurred for 2 years.

This study was approved by the Ethical Review Committee of Peking University People's Hospital. Written informed consent was obtained from the patient for publication.

Discussion

EGPA has traditionally been described to evolve through a prodromic phase, an eosinophilic phase, and a vasculitic phase.[8] Common clinical manifestations of EGPA depend on the timing of diagnosis and stages of disease. The most frequent clinical manifestations of EGPA are respiratory tract involvement. However, patients with EGPA often suffer from intractable sinusitis and sometimes have otological symptoms.[9] A study of 21 patients who were diagnosed with EGPA showed that 52.4% of them showed otological symptoms and 85.7% showed nasal symptoms.[10] These patients also commonly presented with mild-to-moderate mixed or sensorineural hearing loss and showed a high incidence of nasal polyps. Corticosteroids are the cornerstone of treatment for Churg–Strauss syndrome. Corticosteroids are usually sufficient for treating most patients without poor prognosis factors (FFS = 0).[11] Our patient still suffered from aural fullness, nasal obstruction, and rhinorrhea even after receiving adequate medical treatment, including prednisolone, cyclophosphamide, and mycophenolate mofetil. Therefore, we attempted to relieve her symptoms with surgery and topical medication on the basis of systemic therapy.

Postauricular (PA) steroid administration is popular for treating sudden sensorineural hearing loss, Meniere disease, otitis media with effusion (OME), and tinnitus in China.[12,13] PA steroid administration can avoid many side effects resulting from systemic and intratympanic steroids, such as partial inhibition of the hypothalamic–pituitary–adrenal axis, increased blood glucose levels or blood pressure, and persistent tympanic membrane perforation, and have satisfactory therapeutic effects. A study by Wang et al.[14] showed that PA administration resulted in higher dexamethasone concentrations in the perilymph and cochlear tissues than intraperitoneal administration in guinea pigs. In view of the extremely close relationship between the middle ear and inner ear regarding the anatomical position and blood supply, we speculate that PA should also have therapeutic effects on middle ear diseases. Intratympanic injection with steroids for patients with OME has advantages in improving long-term therapeutic efficacy.[15] PA and intratympanic administration of steroids are effective treatments for OME, although there have been no large, randomized, controlled studies on these treatments. In this case, we

used PA steroid administration instead of intratympanic administration after the ventilation tubes dislodged and finally achieved a good continuous treatment effect.

Mucosal edema caused by infection and allergy is a major cause of sinusitis. The key to treating sinusitis is to relieve inflammation and edema of the mucosa. The current conservative therapy for sinusitis mainly consists of antibiotics and topical steroids. Budesonide is a topical applied glucocorticoid, which is widely used in clinical prevention and treatment of asthma, laryngitis, and other respiratory abnormalities. Intranasal budesonide is effective for sinusitis and does not suppress the hypothalamus–pituitary–adrenal axis in sprays, rinses, or respules.[16] However, standard nasal sprays may not deliver medication widely in the sinonasal cavity. Nonstandard topical steroids, which include steroid rinses and intranasal steroid drops, are an option for managing chronic rhinosinusitis.[17] Some studies support the effectiveness of budesonide nasal irrigation in patients with chronic rhinosinusitis, especially those with eosinophilic chronic rhinosinusitis after endoscopic sinus surgery.[18,19] Our patient had EGPA with chronic sinusitis and initially showed eosinophilia and asthma. Therefore, we used budesonide nasal irrigation after surgery instead of traditional nasal sprays, and this was beneficial in postoperative management of the patient.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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