The Challenge of Treating Pulmonary Vasculitis in Behçet Disease: Two Pediatric Cases

Selcan Demir, MD; Erdal Sag, MD; Ummusen Kaya Akca, MD; Tuncay Hazirolan, MD; Yelda Bilginer, MD; Seza Ozen, MD

Behçet disease (BD) is a multisystemic autoinflammatory disorder characterized by recurrent mucocutaneous, ocular, musculoskeletal, gastrointestinal, central nervous system, and vascular manifestations. Pulmonary arterial involvement (PAI) of BD is probably the most severe form of vasculitis, at least in children. PAI has a high mortality, morbidity, and recurrence rate. There are limited data regarding treatment and outcomes of pediatric patients with BD with PAI. Herein, we report 2 pediatric patients with BD presented with hemoptysis and support our data with a systematic review. These patients were given immunosuppressive therapy, which covered pulse methylprednisolone followed by oral prednisolone, intravenous cyclophosphamide every 3 weeks for a total of 6 cycles, and interferon-α2a concomitantly. These are the first reported cases in the literature successfully treated with this treatment modality in a complication with 50% mortality. These patients have been followed up for a period of at least 4 years without any vascular recurrence. Pediatricians should be aware that patients with BD may not present with full diagnostic criteria. They should consider BD in a child with PAI to avoid diagnostic delay and start life-saving accurate immunosuppressive treatment.

Pulmonary arterial involvement (PAI) of BD, the most severe complication of BD, the prevalence is <5%. PAI occurs early in the disease course, unlike other arterial involvements. Recent studies have shown that PAI had strong associations with peripheral venous thrombosis, central nervous system thrombosis, and cardiac thrombosis. Despite the increasing awareness of this potentially fatal vasculitis, early diagnosis, and treatment, its mortality is still high. Data regarding the treatment and outcomes of pediatric patients with PAI are limited.

Herein, we report 2 pediatric patients with BD presenting with PAI and treated successfully with aggressive immunosuppressive treatment (Table 1).
CASE 1

In December 2012, a 15-year-old boy was referred to our hospital for the evaluation and treatment of thrombosis. Three months before referral, he was admitted to a local hospital with abdominal pain, fever, and fatigue. An abdominal Doppler ultrasonography was performed and revealed stenosis of the vena cava inferior (VCI) with a thrombus. Transthoracic echocardiography (TTE) detected that the thrombus extended from the VCI to the right atrium (RA). Ventilation-perfusion scintigraphy results were consistent with pulmonary thromboembolism. Fibrinolytic therapy and anticoagulant therapy were initiated. The patient’s thrombophilia mutations were screened, and a heterozygote mutation in factor V Leiden and a homozygous mutation in methylenetetrahydrofolate reductase (MTHFR) 1298 and plasminogen activator inhibitor-1 (PAI-1) were detected. When he started to have hemoptysis, he was referred to our hospital for further evaluation. His body temperature was 37.5°C, pulse was 76 beats per minute, respiratory rate was 18 breaths per minute, and arterial blood pressure was 110/55 mm Hg. The physical examination revealed a parasternal 4/6 systolic ejection murmur, a genital ulcer (10 × 10 mm), and hepatomegaly. The lung fields were clear to auscultation. The laboratory findings were as follows: white blood cells (WBCs) were 7900 cells per mm³ with 60% neutrophil, hemoglobin (Hb) was 13.1 g/dL, platelets were 230.000/mm³, C-reactive protein (CRP) was 8.5 mg/dL, and erythrocyte sedimentation rate (ESR) was 90 mm/hour.

TTE revealed a left ventricle ejection fraction of ~60% and a mobile mass seen in the RA apex, which was well circumscribed. The chest and abdominal computed tomography angiography (CTA) revealed bilateral aneurysmatic dilatation with thrombi in the pulmonary arteries and thickening of the pulmonary artery walls, thrombosis in the VCI at the suprahepatic level, and thrombi in the vena hepatica (Fig 1A). Anticoagulant treatment was immediately stopped because he had pulmonary artery aneurysm.

### TABLE 1 Clinical Characteristics of the Patients

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patient 1</th>
<th>Patient 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis of BD, y</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>The initial symptoms of BD</td>
<td>Abdominal pain, fever, and hemoptysis</td>
<td>Cough, intermittent hemoptysis, fever, wt loss, and fatigue</td>
</tr>
<tr>
<td>Age at PAI</td>
<td>At the time of diagnosis</td>
<td>At the time of diagnosis</td>
</tr>
<tr>
<td>Type of PAI</td>
<td>PAA and PAT</td>
<td>PAA</td>
</tr>
<tr>
<td>Time between BD diagnosis and PAI, mo</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Follow-up duration</td>
<td>6 y</td>
<td>4 y</td>
</tr>
<tr>
<td>Oral ulcer</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Genital ulcer</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Pathergy</td>
<td>Negative result</td>
<td>Negative result</td>
</tr>
<tr>
<td>HLA B5</td>
<td>Negative result</td>
<td>Positive result</td>
</tr>
<tr>
<td>Ocular lesions</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Skin involvement</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Other vascular involvement</td>
<td>Suprhepatic VCI, vena hepatica (BCS), and RA</td>
<td>Pulse methylprednisolone (intravenous), prednisolone (po), cyclophosphamide (intravenous), IFN-α2a (subcutaneous), adalimumab (subcutaneous)</td>
</tr>
<tr>
<td>Immunosuppression</td>
<td>Pulse methylprednisolone (intravenous), prednisolone (po), cyclophosphamide (intravenous), IFN-α2a (subcutaneous), azathioprine (po)</td>
<td></td>
</tr>
<tr>
<td>Anticoagulation</td>
<td>Received anticoagulation before referral to our center</td>
<td>-</td>
</tr>
<tr>
<td>Thrombophilia</td>
<td>Factor V Leiden: +/+; MTHFR 677: −/−; MTHFR 1298: +/+; PAI-1: 4g/4G +/+; Antiphospholipid antibodies: Negative</td>
<td></td>
</tr>
<tr>
<td>Laboratory tests at the time of PAI</td>
<td>WBC, cells per mm³ 7900</td>
<td>9300</td>
</tr>
<tr>
<td></td>
<td>Hb, g/dL 15.1</td>
<td>9.4</td>
</tr>
<tr>
<td></td>
<td>Platelets, per mm³ 230.000</td>
<td>332.000</td>
</tr>
<tr>
<td></td>
<td>CRP, g/dL 8.5</td>
<td>4.7</td>
</tr>
<tr>
<td></td>
<td>ESR, mm/h 58</td>
<td>80</td>
</tr>
</tbody>
</table>

po, per oral; −, negative; +, positive.
The results of the pathergy test, human leucocyte antigen (HLA) B5, and HLA B51 were negative. Although he did not have enough revised International Criteria of Behçet Disease (ICBD) criteria, we diagnosed him with BD because he had thrombi in PAA, which is almost pathognomonic. He was given immunosuppressive therapy, with pulse methylprednisolone at a dose of 500 mg for 3 days along with and followed by oral prednisolone at 1 mg/kg per day, intravenous cyclophosphamide at a dose of 500 mg (15 mg/kg) every 3 weeks for a total of 6 cycles, followed by oral azathioprine. Concomitant subcutaneous IFN-α2a was given 2 times per week for 6 months. Within 2 weeks, the cough and fever disappeared and CRP and ESR values normalized. After 1 year, the pulmonary artery aneurysm disappeared and cardiac thrombosis resolved and returned nearly normal. We have been managing the patient with azathioprine for 4 years without recurrence.

CASE 2

A 15-year-old boy was referred to our hospital in July 2014 for the evaluation of fever for >4 months and a thrombus in his RA. He had a 3-month medical history of cough, dyspnea, fever, intermittent hemoptysis, and significant weight loss (14 kg). He had several admissions to different hospitals and had been prescribed antibiotics with the diagnosis of pneumonia. In June 2014, a TTE was performed and detected a mass 20 × 30 mm in size in the right ventricle (RV). With the suspicion of infective endocarditis, broad-spectrum antibiotics were initiated. Later on, he had undergone thrombectomy followed by anticoagulant therapy. The blood and urine cultures (3 times) were sterile. High fever persisted for 3 weeks despite antibiotics together with elevated acute phase reactants. A control TTE revealed a recurrent mass (20 × 20 mm) in the RV. He was referred to our hospital for further evaluation. His body temperature was 38.5°C, blood pressure was 120/85 mm Hg, and heart rate was 104 beats per min. Physical examination revealed acnelike rashes over the face and back, multiple ulcers on the buccal mucosa, bilaterally inspiratory and expiratory wheezing, and a 3/6 systolic ejection murmur at the left upper parasternal area. A CTA confirmed the thrombus in the RA and revealed bilateral multiple aneurysms along the pulmonary artery and its branches and thickening of the pulmonary artery walls (Fig 1B). Laboratory tests revealed 9300 WBCs per mm³ with 80% neutrophils, Hb of 9.4 g/dL, platelets at 332,000/mm³, CRP at 4.7 mg/dL, and ESR at 90 mm/hour. HLA-B51 was positive but the pathergy test was negative. Thrombophilia tests revealed a homozygous mutation in MTHFR 677 and in PAI-1. According to revised ICBD, the patient was diagnosed with BD because of having aphthous ulcers, pseudofolliculitis, and vascular involvement. Intravenous methylprednisolone (500 mg/day) for 3 days was followed by oral prednisolone at a dose of 1 mg/kg per day, which was subsequently tapered. Intravenous cyclophosphamide at a dose of 500 mg (15 mg/kg) was also given every 3 weeks for a total of 6 cycles, followed by oral azathioprine. Concomitant subcutaneous IFN-α2a was given 2 times per week for 6 months. Within 2 weeks, the cough and fever disappeared and CRP and ESR values normalized. After 1 year, the pulmonary artery aneurysm disappeared and cardiac thrombosis resolved and returned nearly normal. We have been managing the patient with azathioprine for 4 years without recurrence.

SYSTEMATIC REVIEW OF THE LITERATURE

We performed a review of the literature using PubMed, combining the main keywords “Behçet’s disease AND Pulmonary involvement; OR BD AND pulmonary artery aneurysm; OR BD
AND Pulmonary artery thrombus.” The searches were limited to English language and pediatric patients. Randomized and nonrandomized controlled trials, observational studies (case-control, cohort studies, and case series), and single case reports involving the pediatric patients with BD with pulmonary involvement were included. The references for these studies and review articles for additional publications were also reviewed (Table 2). The author S.D. searched the literature and manually evaluated the titles and abstracts for relevance. Inconsistencies were resolved by discussion with the authors S.O. and Y.B. (Fig 2).

DISCUSSION

We presented 2 pediatric patients with pulmonary involvement of BD and treated the disease successfully with aggressive immunosuppressive treatment.

BD is a multisystemic inflammatory disorder and usually diagnosed in young men; however, it can occur in childhood as well. Previously, International Study Group (ISG) and later on ICBD criteria have been used to diagnose BD; however, both criteria sets were developed for adult patients. Because there are different disease characteristics in adult and pediatric patients with BD, in 2015, an international expert consensus group suggested new classification criteria for pediatric Behçet disease (PEDBD).12 According to this novel PEDBD criteria, all symptom categories have the same weight, and oral aphthosis is not a mandatory criterion anymore. The patient should have 3 or more of the following criteria to be classified as having BD: oral aphthosis (≥3 attacks per year), genital aphthosis (typical with scars), skin involvement (necrotic folliculitis, acneiform lesions, erythema nodosum), neurologic involvement (except isolated headaches), ocular manifestations (anterior uveitis, posterior uveitis, retinal vasculitis), and vascular signs (venous thrombosis, arterial thrombosis, arterial aneurysms).12

Although the patient in case 1 did not have enough PEDBD criteria, the patient in case 2 fulfilled PEDBD criteria with recurrent oral aphthosis, skin involvement, and vascular involvement. The first symptoms of BD may present at early ages; however, all of the criteria for BD diagnosis may not be fulfilled before 16 years of age in more than 80% of patients.13 Koné-Paut et al14 reported 86 children diagnosed with BD and 21 of them failed to fulfill the ISG criteria of BD. Children who are strongly suspected of having BD (eg, who have the pathognomonic finding of PAA with thrombi) and do not fulfill the diagnostic criteria can still be diagnosed as having BD. It is important to include BD in the differential of pulmonary thrombi and aneurysms because early diagnosis and prompt treatment will be lifesaving. Thus, the pediatricians must be aware that patients may not always fulfill the criteria.

BD may involve any size of vessel in both the arterial and venous systems leading to the formation of thrombosis, stenosis, and aneurysms.15 In a multicenter study of 86 children with BD, arterial and venous involvement (except cerebral venous sinus thrombosis) were present in 7% and 12% of the patients, respectively.14 Together with PAl, the patient in case 1 had genital ulcer, cardiac thrombosis, and Budd-Chiari syndrome (BCS), and the patient in case 2 had oral ulcers, pseudofolliculitis, and cardiac thrombosis at the same time. Similar to that, the diagnosis of BD and PAl had been done concomitantly in 5 patients reviewed from the literature.6,7,9,10 When their medical histories were evaluated retrospectively, other features supporting BD were identified except in 1.6 Cohle and Colby6 presented a 10-year-old African American boy who presented with massive hemoptysis and died in a short time period at the hospital. At autopsy, this patient had bilateral inflammatory aneurysms of the lower lobe branches of the pulmonary arteries.6 Microscopic examination in both pulmonary arteries revealed necrotizing lymphocytic vasculitis. There were organized and recanalized thromboembolisms in segmental pulmonary artery branches. He did not have oral or genital ulcerations or eye and skin lesions. Although he did not fulfill the ISG, ICBD, or PEDBD criteria, he was diagnosed with BD on the basis of the autopsy findings.6

The most important type of vascular involvement in BD is the PAl, especially, PAAs, because of its high mortality rate and poor prognosis.16 Koné-Paut et al14 reported that 3 of 86 children with BD had PAl. Unlike other arterial involvements of BD, PAl usually occurs early in the disease course with a male predominance.4,17–19 Consistent with these, our 2 patients and all of the reviewed patients from the literature except 1 were male.11 The most common initial symptom of PAl is hemoptysis and is followed by cough, fever, dyspnea, and chest pain.10 Both of our patients and 6 cases from the literature presented with hemoptysis.5–7,9,10 It has been shown that the mortality ratio for the 14- to 24-year-old age group with BD is 10 times higher than that of the general population. Most of this mortality is related to vascular thrombosis and especially PAA.20 PAl has a poor prognosis. In a previous retrospective study of adult patients with BD, the mortality was 50% among 24 patients with PAA within 1 year after the onset of hemoptysis.18 Seyahi et al10 reported that in 47 adult patients with BD with PAl after a mean follow-up of 7 years,
<table>
<thead>
<tr>
<th>Sex</th>
<th>Male</th>
<th>Male</th>
<th>Male</th>
<th>Male</th>
<th>Male</th>
<th>Male</th>
<th>Male</th>
<th>NA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at BD diagnosis, y</td>
<td>14</td>
<td>10</td>
<td>14</td>
<td>10</td>
<td>17</td>
<td>17</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Initial symptom of PAI</td>
<td>Hemoptysis</td>
<td>Hemoptysis</td>
<td>Fever, wt loss, oral ulcers, and hemoptysis</td>
<td>NA</td>
<td>Hemoptysis, chest pain, fever, and fatigue</td>
<td>Hemoptysis, chest pain, cough, sputum, wt loss, and abdominal pain</td>
<td>Hemoptysis</td>
<td>NA</td>
</tr>
<tr>
<td>ISG criteria</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>ICBD (revised)</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>PEDBD criteria</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Age at PAI, y</td>
<td>17</td>
<td>10</td>
<td>14</td>
<td>15</td>
<td>17</td>
<td>17</td>
<td>12</td>
<td>NA</td>
</tr>
<tr>
<td>Time frame between BD diagnosis and PAI, mo</td>
<td>48</td>
<td>0</td>
<td>0</td>
<td>60</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Type of pulmonary involvement</td>
<td>PAA</td>
<td>PAA</td>
<td>PAA</td>
<td>PAA</td>
<td>PAA</td>
<td>PAT</td>
<td>PAA</td>
<td>PAA</td>
</tr>
<tr>
<td>Other vascular involvement</td>
<td>Cardiac thrombus</td>
<td>Cardiac thrombus</td>
<td>DVT</td>
<td>Hepatic vein thrombosis-BCS</td>
<td>NA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pathergy</td>
<td>NA</td>
<td>NA</td>
<td>+</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Oral ulcer</td>
<td>+</td>
<td>–</td>
<td>+</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>Genital ulcer</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>Eye lesion</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>Skin lesions</td>
<td>Erythema nodosum</td>
<td>Papulopustular lesions</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>Erythema nodosum</td>
<td>Erythema nodosum</td>
<td>NA</td>
</tr>
<tr>
<td>HLA-B5</td>
<td>Positive</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Immunosuppressive treatment</td>
<td>Pulse methylprednisolone (intravenous), prednisolone (po), cyclophosphamide (intravenous)</td>
<td>Colchicine, pulse methylprednisolone (intravenous), prednisolone (po), cyclophosphamide (intravenous)</td>
<td>cyclophosphamide</td>
<td>Corticosteroid, colchicum</td>
<td>Corticosteroid</td>
<td>Prednisolone, cyclophosphamide (intravenous), infliximab (subcutaneous)</td>
<td>Prednisolone, cyclophosphamide (intravenous), infliximab (subcutaneous)</td>
<td>NA</td>
</tr>
<tr>
<td>Anticoagulation</td>
<td>–</td>
<td>–</td>
<td>+ (after resolution of hemoptysis)</td>
<td>NA</td>
<td>–</td>
<td>Enoxaparin + coumadin</td>
<td>–</td>
<td>NA</td>
</tr>
<tr>
<td>Follow-up and outcome</td>
<td>18-mo follow-up with no vascular relapse</td>
<td>Dead before diagnosis because of massive hemoptysis</td>
<td>7-mo follow-up with no vascular relapse</td>
<td>Dead after 2 y of diagnosis because of massive hemoptysis</td>
<td>Dead at 16 mo because of massive hemoptysis</td>
<td>Alive at 7 mo</td>
<td>Dead at 12 mo because of hepatic failure</td>
<td>NA</td>
</tr>
</tbody>
</table>

DVT, deep venous thrombosis; po, per oral; NA, not available.
the mortality rate was 26% and the recurrence rate was 20%. Data regarding treatment and outcomes of pediatric patients with pulmonary artery involvement are limited, and only a few pediatric cases have been reported with this pathology in the literature.

The other main type of pulmonary artery involvement is pulmonary artery thrombus (PAT). PAT could occur with or without PAA. Hemoptysis is also the main presenting symptom in PAT; however, it is less likely to be severe than PAA. Other clinical features are similar in both conditions.\textsuperscript{3,10} Uzun et al\textsuperscript{9} showed that the prognosis of patients with BD with PAI presenting as isolated PAT was better than the prognosis presenting with PAA. However, Seyahi et al\textsuperscript{10} demonstrated that the mortality rate was similar for patients with PAA (26%) and for patients with isolated PAT (23%).

PAT is strongly associated with other venous involvements, such as lower-extremity deep venous thrombosis, cerebral venous sinus thrombosis, and intracardiac thrombosis.\textsuperscript{4} Cardiac thrombosis is mostly located on the right side of the heart and adhered to the endocardium or myocardium.\textsuperscript{21}

Both of our patients had concomitant cardiac thrombosis in the RA. Similar to our patients, Vivante et al\textsuperscript{7} presented a 14-year-old Arab boy who had bilateral PAA and right ventricular thrombus at the diagnosis of BD. Alkaabi and Pathare\textsuperscript{8} reported a 15-year-old boy who had PAA and intracardiac thrombosis who was uncompliant to the treatment and died at 24 months because of massive hemoptysis.

It is important to make a fast differential diagnosis in PAI to provide an early and accurate therapy. More than half of the PAs are due to congenital cardiac (such as atrial septal defects, ventricular septal defects, patent ductus arteriosus, and other structural heart defects) and vessel anomalies (such as Ehler-Danlos syndrome, Marfan syndrome, cystic medial necrosis). However, there are also acquired cases, including infections (tuberculosis, syphilis, endocarditis, septic embolism), pulmonary arterial hypertension, inflammatory lung diseases (bronchiectasis, pulmonary fibrosis, interstitial lung disease), iatrogenic causes (cardiothoracic surgery, pulmonary artery angiography), trauma, and vasculitis (BD, Hughes-Stovin syndrome).\textsuperscript{22}

PAT can be either due to thromboembolic causes (infections, central venous catheters, positivity in thrombophilia mutations, immobilization, surgery, trauma, cancer, inflammatory conditions such as BD, systemic lupus erythematosus, and inflammatory bowel disease) or
due to in situ PAT (local causes such as congenital heart disease, pulmonary artery anomalies, lung transplant). However, thrombi inside the aneurysmatic dilatation of the pulmonary arteries are almost pathognomonic for BD.

BCS is another severe complication of BD and seems to be rare in children. BCS usually presents concomitantly with lower-extremity deep venous thrombosis, iliac vein thrombosis, and intrahepatic VCI thrombosis. It has been shown that the prognosis is better if the patient with BD with BCS presented without ascites. The patient in case 1 presented with PAI and BCS concomitantly. Similar to this patient, Seyahi et al reported a 12-year-old patient who was diagnosed with BD having pulmonary arterial aneurysms and BCS. He had developed hepatic encephalopathy and died of hepatic failure under the treatment prednisolone and cyclophosphamide. No randomized controlled studies evaluating treatment options in pulmonary involvement of BD. The main goal of treatment is to control the inflammation completely; thus, immunosuppressive therapy is essential. PAI is a life-threatening condition and should be managed with more aggressive medical therapy. In 2018, an international group of experts published the European League Against Rheumatism (EULAR)–endorsed recommendations for the management of BD. According to these recommendations, treatment should be personalized according to age, sex, and type and severity of organ involvement. Colchicine is suggested for ulcers in BD, although it is probably not effective in the prevention or treatment of vasculitis. Again, the aforementioned recommendations suggest for the primary management of PAA and PAT as high-dose glucocorticoids and cyclophosphamide. Cyclophosphamide may be given monthly for 6 or 12 months, and glucocorticoids are usually given as 3 intravenous methylprednisolone pulses followed by oral prednisolone at a dose of 1 mg/kg per day. There is no consensus and evidence for the benefit of anticoagulation treatment in the vasculitis of BD. Although it is clear that the only contraindication of anticoagulation is the presence of PAI because of the risk of rupture, they can still be used for other thrombotic involvement in BD.

In accordance with the literature and EULAR recommendations, our patients had been given pulse methylprednisolone at a dose of 500 mg for 3 days along with and followed by oral prednison at a dose of 1 mg/kg per day, and intravenous cyclophosphamide at a dose of 500 mg every 3 weeks for a total of 6 cycles. We strengthened our immunosuppressive treatment with IFN-α2a.

IFN-α2a is successfully used to treat BS-related uveitis. In addition, it also has been shown beneficial in mucocutaneous and articular manifestations. There is no data in the literature regarding the use of IFN-α2a in PAI treatment along with low-dose cyclophosphamide. Our patients were treated successfully with this treatment modality, and the clinical response was good. There were no mortality or recurrences within the 6- and 4-year follow-up periods.

CONCLUSIONS

Because of its high mortality rate and the need to establish a prompt diagnosis and initiate appropriate treatment, pediatricians should include BD in the differential of adolescents who present with a combination of hemoptysis and oral or genital ulcers. Early and aggressive immunosuppressive therapy may improve prognosis.

REFERENCES


ABBREVIATIONS

BCS: Budd-Chiari syndrome
BD: Behçet Disease
CRP: C-reactive protein
CTA: computed tomography angiography
EULAR: European League Against Rheumatism
Hb: hemoglobin
HLA: human leucocyte antigen
ICBD: International Criteria of Behçet Disease
IFN-α2a: interferon-α2a
ISG: International Study Group
MTHFR: methylenetetrahydrofolate reductase
PAI: pulmonary arterial involvement
PAI-1: plasminogen activator inhibitor-1
PAT: pulmonary artery thrombosis
PEDBD: pediatric Behçet disease
RA: right atrium
TTE: transthoracic echocardiography
VCI: vena cava inferior
WBC: white blood cell


The Challenge of Treating Pulmonary Vasculitis in Behçet Disease: Two Pediatric Cases
Selcan Demir, Erdal Sag, Ummusen Kaya Akca, Tuncay Hazirolan, Yelda Bilginer and Seza Ozen
Pediatrics 2019;144;
DOI: 10.1542/peds.2019-0162 originally published online July 18, 2019;

Updated Information & Services
including high resolution figures, can be found at:
http://pediatrics.aappublications.org/content/144/2/e20190162

References
This article cites 30 articles, 3 of which you can access for free at:
http://pediatrics.aappublications.org/content/144/2/e20190162#BIBL

Subspecialty Collections
This article, along with others on similar topics, appears in the following collection(s):
Rheumatology/Musculoskeletal Disorders
http://www.aappublications.org/cgi/collection/rheumatology:musculoskeletal_disorders_sub
Collagen Vascular & Other Multisystem Disorders
http://www.aappublications.org/cgi/collection/collagen_vascular_other_multisystem_disorders_sub

Permissions & Licensing
Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
http://www.aappublications.org/site/misc/Permissions.xhtml

Reprints
Information about ordering reprints can be found online:
http://www.aappublications.org/site/misc/reprints.xhtml
The Challenge of Treating Pulmonary Vasculitis in Behçet Disease: Two Pediatric Cases
Selcan Demir, Erdal Sag, Ummusen Kaya Akca, Tuncay Hazirolan, Yelda Bilginer and Seza Ozen
Pediatrics 2019;144;
DOI: 10.1542/peds.2019-0162 originally published online July 18, 2019;

The online version of this article, along with updated information and services, is located on the World Wide Web at: http://pediatrics.aappublications.org/content/144/2/e20190162

Pediatrics is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. Pediatrics is owned, published, and trademarked by the American Academy of Pediatrics, 345 Park Avenue, Itasca, Illinois, 60143. Copyright © 2019 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 1073-0397.