program specifies new timelines (effective October 1, 2014) for the review of applications for generic drugs in exchange for user fees; by 2017, regulatory action will be required on 90% of new applications for generic drugs within 10 months after submission. The Office of Generic Drugs also expedites applications for generic drugs that are critical to public health or have the potential to mitigate drug shortages.[3]

The FDA has a long track record of successfully meeting the requirements of user-fee programs for the review of drugs, and we are well on our way to meeting the GDUFA commitments. Although no provision exists in the GDUFA for waiving user fees for the review of generic drugs — even for drugs of which there are shortages — having firm timelines in place will allow markets to adjust more quickly to pricing anomalies.

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No potential conflict of interest relevant to this letter was reported.

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THE AUTHORS REPLY: When prices of generic drugs are high because fewer manufacturers make these products, appropriate policy solutions can facilitate the reestablishment of strong, competitive markets. The FDA's move to reduce review times for applications is one such policy. It could also help for Congress to authorize fee waivers for entrants into generic-drug markets in which there are shortages of raw materials or similar factors contributing to exits from the market or price increases, although the current user fee for applications for generic drugs ($58,730) is small as compared with those for new drugs ($2,335,200) or high-risk medical devices ($250,895). However, exorbitant generic-drug prices can have other causes (e.g., demand may fluctuate or improper business practices may reduce competition artificially).[1] In response, the federal government could offer long-term purchasing contracts for some generic drugs, as it does for childhood vaccines, and policymakers should enhance the ability of state and federal government payers to respond to high prices.[2,3] An array of interventions may be needed to ensure that essential generic medications will continue to be available to and affordable for the patients who need them.

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Since publication of their article, the authors report no further potential conflict of interest.

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Sweet's Syndrome in Patients with MDS and *MEFV* Mutations

TO THE EDITOR: We report the finding of *MEFV* mutations in two Japanese patients with the myelodysplastic syndrome (MDS) and skin lesions that are consistent with Sweet's syndrome (acute febrile neutrophilic dermatosis). Both patients had heterozygous mutations in *MEFV*, which are known to cause familial Mediterranean fever.[1,2]

Patient 1, a 63-year-old man with an 8-month history of MDS, was admitted with high fever (temperature, 39.2°C), leukocytosis, and transfusion-dependent anemia. Patient 2, a 63-year-old woman with a 3-month history of MDS, had general malaise on admission, along with anemia and thrombocytopenia. Patient 1 had an

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Case Report

Efficacy of Adalimumab in a Girl with Refractory Intestinal Behcet's Disease

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Academic Editor: Lothar Krause

We describe our experience with a juvenile patient who had refractory intestinal Behcet's disease that responded to adalimumab, a fully humanized antibody against soluble TNF-α and its receptor. The patient, a 13-year-old girl, presented with oral aphthous ulcers, vulvar pain, and rashes on the lower extremities. She gradually developed a low-grade fever, abdominal pain, diarrhea, and hematochezia. Lower gastrointestinal endoscopy revealed ulcers in the terminal ileum, consistent with intestinal Behcet's disease. Methylprednisolone pulse therapy was initiated, after which the symptoms transiently improved, but, during the corticosteroid taper, the abdominal pain recurred. The symptoms resolved soon after the administration of adalimumab. Of importance, the dose of corticosteroids was successfully reduced without exacerbation during 8 months of observation. This is the first reported case in which adalimumab was used for pediatric gastrointestinal Behcet's disease. Adalimumab is a good choice for intestinal Behcet's disease refractory to conventional treatment.

1. Introduction

Behcet's disease is a chronic relapsing vasculitis that is characterized by recurrent oral aphthous and genital ulcers with uveitis [1]. In addition to the main symptoms, there are some much less common manifestations, such as gastrointestinal or central nervous system disease. Pediatric Behcet's disease occurs in approximately 0.3 cases per 100,000 amongst Japanese children [2]. Although the etiology of Behcet's disease is still unknown, studies have revealed an association between tumor necrosis factor-alpha (TNF-α) and the clinical features, and the efficacy of some anti-TNF agents is reported in Behcet's disease patients [3]. We report on a juvenile patient with corticosteroid-dependent intestinal Behcet's disease who responded to subcutaneous adalimumab injections.

2. Case Report

The patient, a 13-year-old girl, had a second-generation Korean father, a Japanese mother, an elder brother, and a younger sister. There was no family history of autoimmune disease. The patient was admitted to our hospital for acute tonsillitis a year before the current admission. She had oral aphthosis recurring more than three times in 12-month period and repeated genital aphthosis. The patient sought evaluation at our hospital for oral ulcers, vulvar pain, headaches, arthralgias, and erythema on the lower extremities in June 2013. She was admitted to the dermatology department. Following the gradual onset of abdominal pain and bloody diarrhea (Figure 1), she was referred to the pediatric department. On admission, the patient had a temperature of 36.2°C, a heart rate of 81 beats per minute, and a blood pressure of 130/86 mmHg. At the time of admission, her physical findings were appropriate for her age, but she lost 2.2 kg during the first week while being admitted to the dermatology department. Edematous erythema and erythema-nodosum-like eruptions were noted on the lower extremities (Figure 2). There were painful ulcers on the left buccal mucosa and left labia minora. Blood testing revealed a significant elevation of the white blood cell count ($14.17 \times 10^3/\mu$L) and C-reactive

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BMC Gastroenterology

CASE REPORT Open Access

Novel exonic mutation inducing aberrant splicing in the *IL10RA* gene and resulting in infantile-onset inflammatory bowel disease: a case report

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Abstract

Background: Although deleterious mutations in interleukin-10 and its receptor molecules cause severe infantile-onset inflammatory bowel disease, there are no reports of mutations affecting this signaling pathway in Japanese patients. Here we report a novel exonic mutation in the *IL10RA* gene that caused unique splicing aberrations in a Japanese patient with infantile-onset of inflammatory bowel disease in association with immune thrombocytopenic purpura and a transient clinical syndrome mimicking juvenile myelomonocytic leukemia.

Case presentation: A Japanese boy, who was the first child of non-consanguineous healthy parents, developed bloody diarrhea, perianal fistula, and folliculitis in early infancy and was diagnosed with inflammatory bowel disease. He also developed immune thrombocytopenic purpura and transient features mimicking juvenile myelomonocytic leukemia. The patient failed to respond to various treatments, including elemental diet, salazosulfapyridine, metronidazole, corticosteroid, infliximab, and adalimumab. We identified a novel mutation (c.537G > A, p.T179T) in exon 4 of the *IL10RA* gene causing unique splicing aberrations and resulting in lack of signaling through the interleukin-10 receptor. At 21 months of age, the patient underwent allogeneic hematopoietic stem cell transplantation and achieved clinical remission.

Conclusions: We describe a novel exonic mutation in the *IL10RA* gene resulting in infantile-onset inflammatory bowel disease. This mutation might also be involved in his early-onset hematologic disorders. Physicians should be familiar with the clinical phenotype of IL-10 signaling defects in order to enable prompt diagnosis at an early age and referral for allogeneic hematopoietic stem cell transplantation.

Keywords: IL-10, IL-10 receptor, infantile-onset inflammatory bowel disease, hematopoietic stem cell transplantation

Background

Interleukin-10 (IL-10), an anti-inflammatory cytokine, binds to 2 receptors, namely 2 alpha molecules (IL-10RA/IL-10R1) and 2 beta molecules (IL-10RB/IL-10R2) [1, 2]. IL-10 signaling plays a key role in maintaining immune homeostasis in the gastrointestinal tract. Accordingly, defects of *IL10*, *IL10RA*, or *IL10RB* genes cause very early-onset inflammatory bowel disease (IBD) including infantile-onset IBD (IOIBD) [3–5]. Patients with mutations in *IL10* or IL10 receptor (*IL10R*) genes present with severe colitis, perianal disease and folliculitis manifesting in the first months of life. These patients are refractory to immunosuppressive therapies such as corticosteroids, methotrexate, thalidomide, and anti-tumor necrosis factor-alpha (TNF-α) antibodies, yet, allogeneic hematopoietic stem cell transplantation (HSCT) has been shown to be curative in these conditions [3–5]. To date over 40 patients of various ethnicities with *IL10*/*IL10R* deficiency have been reported

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ORIGINAL RESEARCH

The 2015 IUIS Phenotypic Classification for Primary Immunodeficiencies

Aziz Bousfiha[1] · Leïla Jeddane[1] · Waleed Al-Herz[2,3] · Fatima Ailal[1] · Jean-Laurent Casanova[4,5,6,7,8] · Talal Chatila[9] · Mary Ellen Conley[4] · Charlotte Cunningham-Rundles[10] · Amos Etzioni[11] · Jose Luis Franco[12] · H. Bobby Gaspar[13] · Steven M. Holland[14] · Christoph Klein[15] · Shigeaki Nonoyama[16] · Hans D. Ochs[17] · Eric Oksenhendler[18,19] · Capucine Picard[5,20] · Jennifer M. Puck[21] · Kathleen E. Sullivan[22] · Mimi L. K. Tang[23,24,25]

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Abstract There are now nearly 300 single-gene inborn errors of immunity underlying phenotypes as diverse as infection, malignancy, allergy, auto-immunity, and auto-inflammation. For each of these five categories, a growing variety of phenotypes are ascribed to Primary Immunodeficiency Diseases (PID), making PIDs a rapidly expanding field of medicine. The International Union of Immunological Societies (IUIS) PID expert committee (EC) has published every

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ORIGINAL RESEARCH

Primary Immunodeficiency Diseases: an Update on the Classification from the International Union of Immunological Societies Expert Committee for Primary Immunodeficiency 2015

Capucine Picard[1,2] · Waleed Al-Herz[3,4] · Aziz Bousfiha[5] · Jean-Laurent Casanova[1,6,7,8,9] · Talal Chatila[10] · Mary Ellen Conley[6] · Charlotte Cunningham-Rundles[11] · Amos Etzioni[12] · Steven M. Holland[13] · Christoph Klein[14] · Shigeaki Nonoyama[15] · Hans D. Ochs[16] · Eric Oksenhendler[17,18] · Jennifer M. Puck[19] · Kathleen E. Sullivan[20] · Mimi L K. Tang[21,22,23] · Jose Luis Franco[24] · H. Bobby Gaspar[25]

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Abstract We report the updated classification of primary immunodeficiencies compiled by the Primary Immunodeficiency Expert Committee (PID EC) of the International Union of Immunological Societies (IUIS). In the two years since the previous version, 34 new gene defects are reported in this updated version. For each disorder, the key clinical and laboratory features are provided. In this new version we continue to see the increasing overlap between immunodeficiency, as

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Decreased levels of inflammatory cytokines in immunoglobulin-resistant Kawasaki disease after plasma exchange

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ABSTRACT

The pathogenesis of coronary artery aneurysm (CAA) formation in Kawasaki disease (KD) remains unknown. However, inflammatory cytokines are thought to play an important role in KD. Patients with intravenous immunoglobulin (IVIG)-resistant KD are more likely to develop CAA. For such refractory patients, steroids and emerging infliximab (IFX) are used; however, further verification is required for their efficacy and safety. Plasma exchange (PE), which removes various inflammatory cytokines, has been used in Japan for over 15 years to prevent CAA in IVIG-resistant KD patients. The sequential change in inflammatory cytokines during the time course of PE has yet to be investigated. In this study, we measured plasma levels of 13 cytokines in nine children with IVIG-resistant KD before the start of PE (day 0: D0), as well as at 1 or 2 days (D1/2), and 4 or 5 days (D4/5) after starting PE. The median age of onset was 8 months (range: 3–53 months). Before PE, patients were treated with IVIG (median dose: 4 g/kg, range: 3–4 g/kg). The median starting period of PE was 8 days after the onset of fever (range: 6–21 days), while its duration was 3 days (range: 2–5 days). Among the 13 cytokines, interleukin-6, tumor necrosis factor-α, tumor necrosis factor receptor I (TNFR1), TNFR2, granulocyte colony-stimulating factor, and IL-17 were significantly lower at D4/5 compared with D0 and/or D1/2, reflecting the potential central efficacy of PE. While three patients developed moderate CAA, their condition regressed within 1 year. The removal of inflammatory cytokines could be the central efficacy of PE against refractory KD.

1. Introduction

Kawasaki disease (KD) is one of the most common forms of vasculitis in children. The annual incidence of KD in Japan increased by 17% from 2005 to 2008. In recent years, nearly 12,000 new cases have been reported each year [1].

Coronary artery aneurysm (CAA) is a critical complication of KD, and develops during the acute phase of the disease. CAA is associated with high morbidity and mortality because of myocardial ischemia, infarction, and sudden death [2]. The use of intravenous immune globulin (IVIG) in combination with aspirin has been proven to be effective in reducing the risk of CAA formation. However, in the absence of IVIG treatment, approximately 20% of KD patients develop CAA [3]. Unfortunately, 10–20% of KD patients show resistance to IVIG and are at higher risk of developing CAA [4,5]. For IVIG-resistant patients, corticosteroids [6], infliximab (IFX) [7], cyclosporine [8], and plasma exchange (PE) [9] are used as alternative therapies. Although corticosteroids have been used for many years, their efficacy, especially in the later days of illness after onset, is still controversial [10,11]. IFX has emerged as a promising therapeutic option in recent years, but its efficacy and safety have yet to be verified.

To date, the pathogenesis of KD is still not been fully elucidated. Activation of innate and adaptive immune systems is thought to be a central feature of KD. There have been many reports on elevation of plasma levels of multiple inflammatory cytokines, such as tumor necrosis factor-α (TNF-α), interleukin (IL)-1β, IL-6, IL-8, and interferon (IFN)-γ, during the acute phase of KD. TNF-α was found to play a major role in the development of CAA in a mouse model of KD [12–19]. Because PE can remove excessive inflammatory cytokines in the circulation [20], its use in IVIG-resistant KD

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Mod Rheumatol. 2015 Jun 13:1-3. [Epub ahead of print]

CINCA syndrome with surgical intervention for valgus deformity and flexion contracture of the knee joint: A case report.

Harada Y[1], Fukiage K, Nishikomori R, Suzuki S, Futami T.

Author information

Abstract

Chronic infantile neurological, cutaneous, and articular (CINCA) syndrome is a systemic autoinflammatory disease caused by increased production of interleukin (IL)-1β. We present a case of CINCA syndrome followed up to skeletal maturity. Joint contracture and valgus deformity of the knee had developed before diagnosis. Surgical interventions by soft tissue release and hemiepiphysiodesis improved the contracture and the deformity, and IL-1 receptor antagonist dramatically controlled systemic inflammation, and the patient lives without any disabilities.

KEYWORDS: CINCA syndrome; Flexion contracture; Hemiepiphysiodesis; IL-1 beta inhibitor

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Mod Rheumatol. 2015 Jan;25(1):1-10. doi: 10.3109/14397595.2014.902747. Epub 2014 May 20.

Pathogenesis of systemic inflammatory diseases in childhood: "Lessons from clinical trials of anti-cytokine monoclonal antibodies for Kawasaki disease, systemic onset juvenile idiopathic arthritis, and cryopyrin-associated periodic fever syndrome".

Yokota S[1], Kikuchi M, Nozawa T, Kanetaka T, Sato T, Yamazaki K, Sakurai N, Hara R, Mori M.

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Abstract

Inflammation has often been considered to be a nonspecific response and to play a bridging role in the activation of adaptive immunity. However, it is now accepted that inflammation is the product of an independent innate immune system closely linked to the adaptive immune system. The key mediators of inflammation are inflammatory cytokines, as determined by multiple lines of evidence both in vitro and in vivo. Due to the crucial role of inflammatory cytokines in the pathogenesis of autoimmune disorders, anti-cytokine treatment has been developed as a therapy for rheumatoid arthritis juvenile idiopathic arthritis (JIA), and inflammatory bowel diseases. We recently completed several clinical trials of anti-cytokine treatment for children with systemic inflammatory diseases: anti-IL-6 receptor monoclonal antibody (tocilizumab) for children with two subtypes of JIA (poly-JIA and systemic JIA), anti-TNF-α monoclonal antibody (infliximab) for children with Kawasaki disease, and anti-IL-1-β monoclonal antibody (canakinumab) for children with cryopyrin-associated periodic syndrome. This review summarizes the basis of inflammation in terms of innate immunity and adaptive immunity in these systemic inflammatory diseases, clinical efficacy, and tolerability of these biologic agents, and attempts to determine the roles of individual inflammatory cytokines in disease pathogenesis.

KEYWORDS: Kawasaki disease; cryopyrin-associated periodic syndrome; inflammation; innate immunity; systemic-onset juvenile idiopathic arthritis

PMID: 24842480 [PubMed - indexed for MEDLINE]

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Mod Rheumatol. 2015 May;25(3):335-43. doi: 10.3109/14397595.2014.969916. Epub 2014 Nov 10.

Pediatric Rheumatology Association of Japan recommendation for vaccination in pediatric rheumatic diseases.

Kobayashi I[1], Mori M, Yamaguchi K, Ito S, Iwata N, Masunaga K, Shimojo N, Ariga T, Okada K, Takei S.

Author information

Abstract

Pediatric Rheumatology Association of Japan has developed evidence-based guideline of vaccination in pediatric rheumatic diseases (PRDs) as a part of Guideline of Vaccination for Pediatric Immunocompromised Hosts. Available articles on vaccination in both adult rheumatic diseases and PRDs were analyzed. Non-live vaccines are generally safe and effective in patients with PRDs on corticosteroid, immunosuppressant, and/or biologics, although efficacy may be attenuated under high dose of the drugs. On the other hand, efficacy and safety of live-attenuated vaccine for the patients on such medication have not been established. Thus, live-attenuated vaccines should be withheld and, if indicated, may be considered as a clinical trial under the approval by Institutional Review Board. All patients with PRDs anticipating treatment with immunosuppressants or biologics should be screened for infection of hepatitis B and C and tuberculosis before the commencement of medication. Varicella vaccine should be considered in sensitive patients ideally 3 weeks or longer before the commencement of immunosuppressants, corticosteroids, or biologics. Bacille Calmette-Guérin should be withheld at least for 6 months after birth, if their mothers have received anti-tumor necrosis factor-α antibodies during the second or third trimester of pregnancy.

KEYWORDS: Immunosuppression; Pediatric; Rheumatic disease; Vaccine

PMID: 25381726 [PubMed - indexed for MEDLINE]

See 1 citation found by title matching your search:

PLoS One. 2015 May 14;10(5):e0125938. doi: 10.1371/journal.pone.0125938. eCollection 2015.

Identification of Disease-Promoting HLA Class I and Protective Class II Modifiers in Japanese Patients with Familial Mediterranean Fever.

Yasunami M[1], Nakamura H[1], Agematsu K[2], Nakamura A[3], Yazaki M[3], Kishida D[3], Yachie A[4], Toma T[4], Masumoto J[5], Ida H[6], Koga T[7], Kawakami A[7], Eguchi K[8], Furukawa H[9], Nakamura T[10], Nakamura M[11], Migita K[11].

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Abstract

OBJECTIVES: The genotype-phenotype correlation of MEFV remains unclear for the familial Mediterranean fever (FMF) patients, especially without canonical MEFV mutations in exon 10. The risk of FMF appeared to be under the influence of other factors in this case. The contribution of HLA polymorphisms to the risk of FMF was examined as strong candidates of modifier genes.

METHODS: Genotypes of HLA-B and -DRB1 loci were determined for 258 mutually unrelated Japanese FMF patients, who satisfied modified Tel-Hashomer criteria, and 299 healthy controls. The effects of carrier status were evaluated for the risk of FMF by odds ratio (OR). The HLA effects were also assessed for clinical forms of FMF, subsets of FMF with certain MEFV genotypes and responsiveness to colchicine treatment.

RESULTS: The carriers of B*39:01 were increased in the patients (OR = 3.25, p = 0.0012), whereas those of DRB1*15:02 were decreased (OR = 0.45, p = 0.00050), satisfying Bonferroni's correction for multiple statistical tests (n = 28, p<0.00179). The protective effect of DRB1*15:02 was completely disappeared in the co-existence of B*40:01. The HLA effects were generally augmented in the patients without a canonical MEFV variant allele M694I, in accordance with the notion that the lower penetrance of the mutations is owing to the larger contribution of modifier genes in the

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Mod Rheumatol. 2016 Mar;26(2):315-7. doi: 10.3109/14397595.2014.988861. Epub 2014 Dec 22.

IL-18 serum concentration is markedly elevated in typical familial Mediterranean fever with M694I mutation and can distinguish it from atypical type.

Yamazaki T[1,2], Shigemura T[3], Kobayashi N[3], Honda K[4], Yazaki M[5], Masumoto J[6], Migita K[7], Agematsu K[2,3,4].

Author information

KEYWORDS: FMF; IL-18; IL-1β; Inflammasome; Pyrin

PMID: 25528861 [PubMed - in process]

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Mod Rheumatol. 2015 Oct 16:1-4. [Epub ahead of print]

The safety and effectiveness of HBV vaccination in patients with juvenile idiopathic arthritis controlled by treatment.

Nerome Y[1,2], Akaike H[1], Nonaka Y[1], Takezaki T[1], Kubota T[1], Yamato T[1], Yamasaki Y[1], Imanaka H[1], Kawano Y[1], Takei S[1,3].

Author information

Abstract

OBJECTIVES: To evaluate the safety and effectiveness of hepatitis B virus (HBV) vaccination in patients with juvenile idiopathic arthritis (JIA) controlled by treatment.

METHODS: Among 49 patients with juvenile idiopathic arthritis (JIA) at the outpatient clinic of Kagoshima University Hospital, we enrolled 25 who were controlled by treatment. All children were unimmunized and were vaccinated against HBV according to the schedule. Their responses to the vaccine and vaccine adverse events were examined during their visits.

RESULTS: Nineteen of the 25 patients with JIA controlled by treatment developed effective antibody responses (76%). All eight patients with JIA below 10 years of age achieved seroconversion. The seroconversion was not influenced by biologics. Five adverse events were observed (6.7%). The rate of all adverse events did not surpass that of a previous report, and all adverse events were immediately resolved. None of the patients with JIA experienced a flare-up or clinical deterioration related to the vaccination.

CONCLUSIONS: HBV vaccination is safe and effective. Pediatric rheumatologists should consider HBV vaccination for unimmunized patients with JIA, because the response to HBV vaccine might be influenced by age, and children have a higher risk for potential HBV infection than adults.

KEYWORDS: Biologics; Hepatitis B virus; Juvenile idiopathic arthritis; Vaccination

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Mod Rheumatol. 2015 Dec 14:1-6. [Epub ahead of print]

Prediction of long-term remission of oligo/polyarticular juvenile idiopathic arthritis with S100A12 and vascular endothelial growth factor.

Yamasaki Y[1], Takei S[2], Imanaka H[1], Nerome Y[1], Kubota T[1], Nonaka Y[1], Akaike H[1], Takezaki T[1], Kawano Y[1].

Author information

Abstract

OBJECTIVES: This study aimed to evaluate the usefulness of S100A12 and vascular endothelial growth factor (VEGF) for predicting the stability of remission for discontinuing methotrexate (MTX) and/or biological agents in Japanese patients with oligo/polyarticular juvenile idiopathic arthritis (JIA).

METHODS: Forty-four patients with oligo/polyarticular JIA who received MTX with or without biological agents were enrolled. Serum concentration of both S100A12 and VEGF were simultaneously evaluated by ELISA in active and in remission phase determined by activity markers including DAS-28.

RESULTS: S100A12 and VEGF were correlated with DAS-28. Of the 22 patients with oligo/polyarticular JIA in clinical remission, 13 patients with low S100A12 and VEGF concentrations could discontinue treatment without relapse over 2 years. However, nine patients without low S100A12 and VEGF concentrations relapsed afterwards, even though they had been in clinical remission. The cut-off levels of S100A12 and VEGF for division into two groups of the maintenance remission and relapse groups were 177 ng/ml and 158 pg/ml, respectively.

CONCLUSIONS: S100A12 and VEGF are useful markers for assessing disease activity of oligo/polyarticular JIA in remission phase. These markers should be kept low when clinicians consider tapering or discontinuing treatments in oligo/polyarticular JIA patients.

KEYWORDS: DAS-28; Long-term remission; Oligo/polyarticular JIA; S100A12; VEGF

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Mod Rheumatol. 2015 Oct 7:1-4. [Epub ahead of print]

Disease activity score in 28 joints at 3 months after the initiation of biologic agent can be a predictive target for switching to the second biologic agent in patients with polyarticular juvenile idiopathic arthritis.

Kubota T[1], Imanaka H[2], Takei S[2,3], Yamatou T[2], Nerome Y[4], Yamasaki Y[1], Nonaka Y[2], Akaike H[2], Takezaki T[2], Kawano Y[2].

Author information

Abstract

OBJECTIVE: To clarify polyarticular juvenile idiopathic arthritis (pJIA) patients who failed to maintain prolonged remission with the first biologic agent.

METHODS: Fourteen pJIA patients were observed for 47.5 months (median) after initiating the first biologic agent.

RESULTS: Eight maintained sustained clinical remission (median 47 months) with the first biologic agents, while the six switched to the second one due to lack of efficacy, thereafter. Receiver operating characteristic (ROC) analysis revealed that disease activity score in 28 joints (DAS28) of 2.37 at 3 months could distinguish between the two patient groups ($p = 0.001$).

CONCLUSION: pJIA patients with DAS28 >2.37 at 3 months of the initial biologic therapy may be considered to switch to the second biologics.

KEYWORDS: Biologic agent; DAS28; Juvenile idiopathic arthritis; Polyarticular-type; Switching

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Mod Rheumatol. 2015 May;25(3):335-43. doi: 10.3109/14397595.2014.969916. Epub 2014 Nov 10.

Pediatric Rheumatology Association of Japan recommendation for vaccination in pediatric rheumatic diseases.

Kobayashi I[1], Mori M, Yamaguchi K, Ito S, Iwata N, Masunaga K, Shimojo N, Ariga T, Okada K, Takei S.

Author information

Abstract

Pediatric Rheumatology Association of Japan has developed evidence-based guideline of vaccination in pediatric rheumatic diseases (PRDs) as a part of Guideline of Vaccination for Pediatric Immunocompromised Hosts. Available articles on vaccination in both adult rheumatic diseases and PRDs were analyzed. Non-live vaccines are generally safe and effective in patients with PRDs on corticosteroid, immunosuppressant, and/or biologics, although efficacy may be attenuated under high dose of the drugs. On the other hand, efficacy and safety of live-attenuated vaccine for the patients on such medication have not been established. Thus, live-attenuated vaccines should be withheld and, if indicated, may be considered as a clinical trial under the approval by Institutional Review Board. All patients with PRDs anticipating treatment with immunosuppressants or biologics should be screened for infection of hepatitis B and C and tuberculosis before the commencement of medication. Varicella vaccine should be considered in sensitive patients ideally 3 weeks or longer before the commencement of immunosuppressants, corticosteroids, or biologics. Bacille Calmette-Guérin should be withheld at least for 6 months after birth, if their mothers have received anti-tumor necrosis factor-α antibodies during the second or third trimester of pregnancy.

KEYWORDS: Immunosuppression; Pediatric; Rheumatic disease; Vaccine

PMID: 25381726 [PubMed - indexed for MEDLINE]

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Mod Rheumatol. 2015 Apr 30:1-5. [Epub ahead of print]

Protracted arthritis in a Japanese patient with familial Mediterranean fever.

Migita K[1], Hisanaga S, Izumi Y, Kawahara C, Shigemitsu Y, Iwanaga N, Araki T, Kamata M, Izumi M, Kumagai K, Kawakami A.

Author information

Abstract

The most common arthritic involvement in familial Mediterranean fever (FMF) is acute self- limiting monoarthritis which typically lasts for 72 h. Hip joint involvement is uncommon in FMF and can result either from a process specific to this disease or from a coexisting inflammatory joint disease. We describe a 37-year-old woman with FMF and right osteoarthritis secondary to congenital hip dislocation. Periodic fever with right coxalgia lasting for 6 months was treated using colchicine. Genetic analysis revealed homozygous mutation in the MEFV gene (L110P-E148Q/L110P-E148Q), confirming the FMF diagnosis. Although the clinical presentation and course of FMF arthritis are diverse, delineating these clinical patterns may help with early recognition and treatment to prevent destructive arthritis in FMF. Clinicians should consider the possibility of FMF development in unusual monoarthritis patients with recurrent febrile attacks.

KEYWORDS: Colchicine; Congenital hip dislocation; Familial Mediterranean fever; MEFV gene

PMID: 25800639 [PubMed - as supplied by publisher]

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Mod Rheumatol. 2015 Jan;25(1):62-6. doi: 10.3109/14397595.2014.929558. Epub 2014 Jul 14.

Long-term outcome of 114 adult JIA patients in a non-pediatric rheumatology institute in Japan.

Miyamae T[1], Tanaka E, Kishi T, Matsuyama T, Igarashi T, Fujikawa S, Taniguchi A, Momohara S, Yamanaka H.

Author information

Abstract

OBJECTIVE: To evaluate the long-term outcome of patients with juvenile idiopathic arthritis (JIA) using data from a large cohort database, Institute of Rheumatology, Rheumatoid Arthritis, managed by the Tokyo Women's Medical University.

METHODS: Of 182 patients identified from the database from 2000 to 2013, 114 were verified as having JIA. The transition of medical care and the contributions of biological DMARDs were evaluated.

RESULTS: The mean age of the patients (93 females, 81.6%) at the latest examination was 36.6 ± 13.3 years. The mean age at disease onset and mean disease duration were 11.6 ± 3.4 and 25.0 ± 13.3 years, respectively. Of the 114 patients, 106 (93.0%) had poly- or oligoarthritis. Only one-fourth transferred from general pediatricians or pediatric rheumatologists. More patients with recent disease onset were treated with biological DMARDs (16.7% in the 1970s, vs. 80.0% in the 2000s). Disease activity assessed with DAS28 was significantly lower when disease onset was more recent (3.9 ± 1.3 for onset in the 1960s vs. 2.2 ± 1.1 for onset in the 2000s, $p = 0.04$). The percentage of patients requiring orthopedic surgery has decreased (53.8% before the 1970s vs. 10.0% in the 2000s).

CONCLUSION: Patients with more recent disease onset showed an improved outcome. Establishing and sharing a transition program among pediatric and non-pediatric rheumatologists is desirable.

KEYWORDS: Biologic agents; Juvenile chronic arthritis; Juvenile idiopathic arthritis; Juvenile rheumatoid arthritis; Outcome assessment

PMID: 25019624 [PubMed - indexed for MEDLINE]