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CASES WITH A MESSAGE

Juvenile dermatomyositis with IgA nephropathy: case-based review

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Abstract

Juvenile dermatomyositis (JDM) is the most common childhood idiopathic inflammatory myopathy (IIM). It is characterized by the classic skin rash in the form of Gottron papules and heliotrope rash, and symmetric proximal muscle weakness. Renal involvement in JDM is rare which includes acute kidney injury and glomerulonephritis. We report a 10-year-old boy with juvenile dermatomyositis and IgA nephropathy. Child responded dramatically to the conventional therapy with steroids and methotrexate for the primary disease, and did not require any additional treatment for his renal disease. Child's primary disease is in remission and has normal urinalysis with normal renal function at 6-month follow-up. We reviewed the literature and found 11 cases of IIMs with renal involvement. Four patients (one JDM, two polymyositis, and one dermatomyositis) had IgA nephropathy out of which three patients responded to the conventional therapy of primary disease and only one patient with polymyositis needed hiking immunosuppression targeted for renal condition. Therapy targeting the underlying disorder is usually sufficient in patients with JDM and secondary IgA nephropathy.

Keywords Juvenile dermatomyositis · Acute kidney injury · IgA nephropathy

Introduction

Chronic idiopathic inflammatory myopathies (IIMs) are relatively heterogeneous disorders in childhood and Juvenile dermatomyositis (JDM) is the most common childhood IIM [1]. It is characterized by the classic skin rash in the form of Gottron papules and heliotrope rash, and symmetric proximal muscle weakness [1, 2]. Fever, arthritis, dysphagia, dysphonia, muscle tenderness, and fatigue are also commonly reported in JDM [3]. Although onset is insidious, there is a great variation in the rapidity of evolution of clinical manifestations. JDM is an autoimmune disease that, besides skin and muscle, involves other organ systems like joints, gastrointestinal tract, and lungs. Criteria used by Bohan and Peter are still used in the diagnosis of JDM, although their validity in children is unclear, and with the advent of magnetic resonance imaging (MRI) studies, the role of invasive procedures like muscle biopsy for diagnosis of JDM has declined over time [4]. Renal involvement in JDM is rarely reported [5]. Data in adults shows that up to one-fifth of cases of inflammatory myopathies can have renal lesions; however, there are only anecdotal reports of renal involvement in JDM [5].

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Case report

We report a case of 10-year-old boy with juvenile dermatomyositis (JDM) and IgA nephropathy on renal biopsy. The child presented with progressive skin rash, proximal muscle weakness predominantly involving lower extremities, and fever from last 4 years. Fever was low grade (maximum 101 °F), intermittent, occurring every 1–2 months, and each febrile episode would subside within a few days. On examination, the child had stable vitals and no hypertension, and had heliotrope rash, Gottron papules, and scalp dermatitis. On neurological examination, muscle power in lower limbs was 4/5 and upper limbs 5/5. There was no weakness of truncal/axial/neck muscles, and no cranial nerve deficits. Deep tendon reflexes were preserved and sensory examination was unremarkable. Rest of the systemic examination was within normal limits. Laboratory tests showed that hemoglobin 10.9 g/dl, total leukocyte count 10,400/mm^3, platelet count 220,000/mm^3, erythrocyte sedimentation rate (ESR) 55 mm/h (normal < 15 mm/h), c-reactive protein (CRP) 21 mg/l (normal < 6 mg/l), alanine transaminase 32 U/l (normal 7–56 U/l), aspartate transaminase 18 U/l (normal 10–40 U/l), serum creatine phosphokinase 556 mcg/l (normal 40–220), and serum aldolase 30 U/l (normal < 8 U/l). His urine examination showed hematuria (6–8 RBC/hpf) and 2 + proteinuria for 3 consecutive days with normal urine output [2100 ml/24 h (2.5 ml/kg/h)]. Estimation of 24 h urinary protein revealed non-nephrotic range proteinuria (300 mg/day). Renal function tests were normal (urea 21 mg/dl; creatinine 0.4 mg/dl). Serum albumin was 3.4 g/dl (normal 3.5–5.5 g/dl), serum globulin levels 2 g/dl (normal 2–3.5 g/dl), triglycerides 64 mg/dl (normal < 150 mg/dl), total cholesterol 90 mg/dl (normal < 200 mg/dl), LDL cholesterol 60 mg/dl (normal < 130 mg/dl), and HDL cholesterol 20 mg/dl (normal > 60 mg/dl).

We made a diagnosis of juvenile dermatomyositis based on characteristic skin lesions, proximal muscle weakness, elevated CPK levels, and features of myopathy on electromyography (insertional activity and low amplitude, short-duration polyphasic motor potentials). MRI of thigh revealed bilateral hyper-intense gluteal muscles. Possibility of JDM and SLE overlap was also kept in view of proteinuria and hematuria; however, ANA and anti-ds-DNA were negative [ANA < 1:40 and anti-ds-DNA (< 5 IU/ml)]. As it was difficult to explain hematuria and proteinuria on urine examination in the background of JDM, we performed a renal biopsy. Light microscopy of renal biopsy showed mesangial hypercellularity. Immunofluorescence (IF) revealed granular mesangial deposits of IgA(3+), C3(3+), kappa(3+), and lambda(3+); but was negative for IgG, IgM, and C1q, suggestive of mesangioproliferative IgA nephropathy with MEST(C) score M1E0S0T0(C0) (Fig. 1a, b). Nail fold dermoscopy revealed dilated and tortuous nail fold capillaries with ragged cuticle. For JDM, child was treated with IV pulse methyl prednisolone (10 mg/kg/pulse) for 3 days, followed by oral prednisolone (2 mg/kg/day). He became afebrile with improvement in muscle power and general well-being. He was discharged on oral prednisolone (1 mg/kg/day), weekly subcutaneous methotrexate (15 mg/m^2) along with weekly folic acid. On follow-up at 2 weeks, proteinuria and hematuria disappeared completely. Dose of prednisolone was gradually tapered, and on last follow-up at 6 months, he was on daily oral steroid (Prednisolone 0.5 mg/kg/day) with weekly methotrexate. Child had improvement of muscle weakness and skin rashes with no recurrence of proteinuria or hematuria till last follow-up.

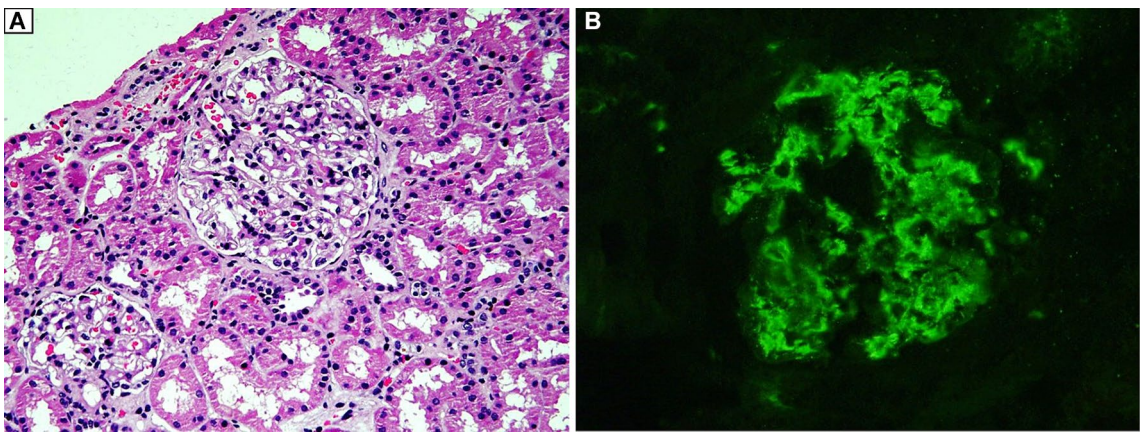

Fig. 1 **a** Glomeruli display mild to moderate mesangial expansion with hypercellularity [hematoxylin and eosin staining (H&E), ×400]. No segmental sclerosis or endocapillary proliferation seen. **b** Immunofluorescence shows mesangial granular deposits of immunoglobulin A (IgA 3+)

Search strategy

We conducted a computerized search of the PubMed, MEDLINE, and Scopus database using combinations of the terms "Juvenile dermatomyositis", "dermatomyositis", "polymyositis", "renal involvement", and "IgA nephropathy". The search period was from database inception to till 14 September 2018. The references of retrieved articles were searched for relevant articles. Eleven cases were found, out of which two cases were of JDM, two cases of Polymyositis (PM), and seven cases of dermatomyositis (DM). Details of relevant cases are summarized in Table 1.

Discussion

Juvenile dermatomyositis is a multisystem connective tissue disorder which may involve kidneys in addition to skin, muscle, joints, GIT, and lungs. Two kinds of renal lesions are described with JDM, which include acute kidney injury (AKI) and glomerulonephritis. AKI results from rhabdomyolysis and myoglobinuria, leading to acute tubular necrosis [5]. Some patients develop glomerulonephritis that appears as hematuria or proteinuria or both which is possibly caused by immune dysregulation. The reported glomerulonephritis with JDM include membranous nephropathy, mesangioproliferative glomerulonephritis, minimal change disease, rapidly progressive glomerulonephritis, and focal segmental glomerulosclerosis [6]. We reviewed the literature and found two cases of JDM associated with renal involvement. Nickavar et al. described a 7-year-old boy with nephrotic syndrome and renal failure with subsequent development of JDM [7]. Similar to our case, a 14-year-old girl with newly diagnosed JDM who had persistent hematuria and proteinuria was found to have IgA nephropathy on renal biopsy. Patient was treated for underlying JDM with prednisolone and methotrexate for 6 weeks followed by tapering of steroid, and no new drug was added for IgA nephropathy [8]. Adult patients with dermatomyositis ($n=7$) and polymyositis ($n=2$) had varied presentation from minimal changed disease to crescentic GN. It is interesting to note that most of them responded well to the conventional immunosuppression. Only one patient with dermatomyositis developed CKD. Both JDM and IgA nephropathy are immune complex-mediated diseases; hence, there may be some common pathogenetic mechanism involved. Such rare associations between autoimmune diseases are known to occur [9].

The underlying pathophysiologic mechanism in IgA nephropathy, the most common primary glomerulonephritis, involves an inherent genetically determined presence of high levels of aberrantly glycosylated IgA1. Auto antibodies against these IgA1 result in immune complex formation, with subsequent deposition in the glomeruli followed by mesangial proliferation and inflammation [10]. IgA nephropathy also occurs in patients with the other systemic diseases like rheumatic disorders, gastrointestinal and liver disorders, respiratory disorders, chronic infections, or certain neoplasms. The exact prevalence of such secondary IgA nephropathy is difficult to estimate. The pathophysiology has also not been fully elucidated in secondary IgA nephropathy [11]. It is also not clear whether such associations with IgA nephropathy are pathologically linked or simply coincidental

Table 1 Summary of case reports of idiopathic inflammatory myopathies with renal involvement

References	Age/sex of patient	IIM	Renal biopsy	Treatment	Outcome
Civilibal et al. [8]	14 years/F	JDM	IgAN	Cs, Mtx	Improved
Nickavar et al. [7]	7 years/M	JDM	Acute renal failure Nephrotic syndrome (NS)	Cs, CyA, IVIG, Plasmapheresis	NS persisted
Yen et al. [5]	26 years/F	DM	IgAN	Cs, AZA	Improved
Barros et al. [14]	35 years/M	PM	IgAN	Cs, AZA, CYC	Improved
Oh et al. [15]	56 years/F	PM	IgAN	Cs, CYC, IVIG	Improved
Machado et al. [16]	51 years/M	DM	Crescentic GN	Cs, CYC	Improved
Yuste et al. [17]	47 years/F	DM	Crescentic GN	Cs, CYC, MMF	Improved
Xie et al. [18]	44 years/M	DM	DPGN	Cs, CYC	Improved
Couvrat et al. [19]	39 years 42 years	DM DM	MCD MCD	Cs, AZA Cs, Mtx, IVIG	CKD improved
Akashi et al. [20]	43 years/F	DM	MN	Cs, CyA	Improved
Our case	10 years/M	JDM	IgAN	Cs, Mtx	Improved

IIM idiopathic inflammatory myopathies, *JDM* juvenile dermatomyositis, *DM* dermatomyositis, *PM* polymyositis, *IgAN* IgA nephropathy, *MN* membranous nephropathy, *MCD* minimal change disease, *DPGN* diffuse proliferative glomerulonephritis, *Cs* corticosteroids, *Mtx* methotrexate, *AZA* azathioprine, *CYC* cyclophosphamide, *CyA* cyclosporine, *MMF* mycophenolate mofetil, *IVIG* intravenous immunoglobulin

findings, as there are reports of mesangial IgA deposits even in healthy asymptomatic individuals [12].

Due to limited data and systemic nature of disease, no guidelines actually exist regarding treatment of glomerulonephritis in these patients as compared to idiopathic form of glomerulonephritis. Management of idiopathic IgA nephropathy includes angiotensin converting enzyme inhibitors and steroids. In patients with JDM with normal renal functions and small degrees of hematuria and proteinuria, treatment regimen of JDM usually takes care of ongoing renal lesion. Our patient also responded well to steroid therapy, and showed resolution of hematuria and proteinuria in 1 week. However, if patient develops nephrotic range proteinuria or worsening of renal function, the addition of other immunosuppressive drugs like cyclophosphamide, azathioprine, cyclosporine, and mycophenolate mofetil should be considered [13]. Although the outcome of idiopathic IgA nephropathy is generally good, progressive disease occurs in 20–30% of patients after 15–20 years of disease onset and, therefore, needs close follow-up [9]. It seems that the immunosuppressive therapy used for underlying JDM is usually sufficient to address the associated IgA nephropathy [13].

Conclusion

Juvenile dermatomyositis may affect the renal system and patients with abnormal urinalysis findings should be further evaluated. Majority of the cases of dermatomyositis with renal involvement respond well to the immunosuppressive therapy given for the primary disease.

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Author contributions MRM: prepared the manuscript. SKT: collected data of patient and reviewed the literature. RHP: pathological part of manuscript was prepared along with review of current and old cases. NKB: edited the manuscript and gave critical inputs for preparation of manuscript. PH: reviewed the draft and final revision of the manuscript. AB: analysis and interpretation of pathological findings of cases and inclusion in the main draft. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Compliance with ethical standards

Conflict of interest All authors declare that there are no conflicts of interest.

Ethical approval This article does not contain any studies on human participants or animals performed by any authors.

Informed Consent Informed consent of parents of patient concerned was taken in an appropriate format.

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