Two emerging phenotypes of atypical inclusion body myositis: illustrative cases

S. Salam[1], J.M. Morrow[1], R. Howard[1,2], J.A.L. Miller[3], R.M. Quinlivan[1], P.M. Machado[1]

[1]Department of Neuromuscular Diseases, UCL Queen Square Institute of Neurology and The National Hospital for Neurology and Neurosurgery, London; [2]Department of Neurology, Guys and St Thomas Hospitals, London; [3]Department of Neurology, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK.

Abstract

Objective

Sporadic inclusion body myositis (IBM) is the most common acquired myopathy in those aged above 50. It is classically heralded by weakness in the long finger flexors and quadriceps. The aim of this article is to describe five atypical cases of IBM, outlining two potential emerging clinical subsets of the disease.

Methods

We reviewed relevant clinical documentation and pertinent investigations for five patients with IBM.

Results

The first phenotype we describe is young-onset IBM in two patients who had symptoms since their early thirties. The literature supports that IBM can rarely present in this age range or younger. We describe a second phenotype in three middle-aged women who developed early bilateral facial weakness at presentation in tandem with dysphagia and bulbar impairment followed by respiratory failure requiring non-invasive ventilation (NIV). Within this group, two patients were noted to have macroglossia, another possible rare feature of IBM.

Conclusion

Despite the classical phenotype described within the literature IBM can present in a heterogenous fashion. It is important to recognise IBM in younger patients and investigate for specific associations. The described pattern of facial diplegia, severe dysphagia, bulbar dysfunction and respiratory failure in female IBM patients requires further characterisation. Patients with this clinical pattern may require more complex and supportive management. Macroglossia is a potentially under recognised feature of IBM. The presence of macroglossia in IBM warrants further study, as its presence may lead to unnecessary investigations and delay diagnosis.

Key words

inclusion body myositis, facial weakness, bulbar, dysphagia, macroglossia, young-onset, atypical, respiratory failure

Sharfaraz Salam, MD
Jasper M. Morrow, FRACP, PhD
Robin Howard, MD, PhD
James A.L. Miller, MD, PhD
Ros M. Quinlivan, MD
Pedro M. Machado, MD, PhD

Please address correspondence to:
Pedro M. Machado,
Department of Neuromuscular Diseases,
1st Floor, Russell Square House,
10-12 Russell Square,
London WC1B 5EH, United Kingdom.
E-mail: p.machado@ucl.ac.uk

Received on January 26, 2023; accepted in revised form on February 13, 2023.

Fundings. S. Salam is supported by a UCL Queen Square Institute of Neurology & Cleveland Clinic London MPhil/PhD Neuroscience Fellowship. P.M. Machado and R.M. Quinlivan are supported by the National Institute for Health Research (NIHR) University College London Hospitals (UCLH) Biomedical Research Centre (BRC).

Competing interests: J.A.L. Miller has participated in Advisory board for Argenx and UCB in 2001. P.M. Machado has received honoraria/consultancies from Abbvie, BMS, Celgene, Eli Lilly, Galapagos, Janssen, MSD, Novartis, Orphazyme, Pfizer, Roche and UCB.
The other authors have declared no competing interests.

Introduction

IBM is the most common acquired myopathy in individuals aged over 50 (1). Although autoimmunity is thought to play a key role in the pathogenesis of IBM, it is clear that abnormal protein homeostasis is an important sequalae of the disease (1-4). The classical clinical picture is that of marked long finger flexor weakness and quadriceps weakness presenting in middle aged individuals (1). In this manuscript we describe two potentially new phenotypes of atypical IBM that deviate from this typical clinical picture and may be under recognised in clinical practice.

Young-onset IBM

Case 1

A 34-year-old man presented to his local tertiary neuroscience centre in 2021. Since the age of 31 he described pain in his extremities and was diagnosed with Raynaud's syndrome. He initially had a normal neurological examination. Blood testing revealed ANA, Ku and PM/Scl seropositivity. There was raised IgG and IgA levels, coupled with reduced complement. He had a mildly raised creatine kinase (CK) of 800 (normal range 26-140 IU/L), however myositis antibody screening was negative. A CT thorax demonstrated splenomegaly.

An upper limb MRI was performed in 2020 followed by repeat imaging of both upper and lower limbs in 2021. This showed evidence of hyperintensity in the upper arm and forearm muscles on T2 weighted short tau inversion recovery (STIR) sequences (Fig. 1). The appearances of MRI lower limb were largely unremarkable apart from mild STIR abnormalities in distal vastus lateralis and tibialis anterior.

Muscle histology from a triceps biopsy revealed features supportive of IBM (Table I). Screening for T-cell large granular lymphocytic leukaemia (T-LGLL) was negative.

In 2022 he reported mild dysphagia and difficulty making a fist. He described discomfort in the thoracic and scapular musculature, with wasting in the paraspinal muscles. On examination he had mild weakness in the long finger flexors (specifically the fourth and fifth digits), thumb abduction and hip flexion (Table I). His forced vital capacity (FVC) was 68% of that predicted. Treatment with mycophenolate and methylprednisolone had no benefit on his muscle symptoms.

Case 2

A 39-year-old woman with a 9-year history of muscle complaints, was referred to our neurosciences centre in 2022. She had a background of coeliac disease, which was well controlled. At the age of 31, she noticed bilateral calf pain. Over the next 5 years she noticed weakness of her grip and difficulty standing up from the floor. She described worsening dysphagia over the past 4 years.

On examination at our centre, she had bilateral facial weakness and tongue wasting. There was severe wasting of anterior forearm muscles and quadriceps. Most marked weakness was in long finger flexion (Table I). Her FVC whilst sitting was 47% of that predicted.

The patient had undergone detailed investigations over the past few years. Testing via the 100,000-genome project did not identify variants of significance. This project was established within the United Kingdom to identify pathogenic genomic variants in rare diseases. A borderline positivity for acetylcholine receptor antibody was noted on two occasions in 2022, 1.02 and 1.55 (normal range 0-0.45 nmol/L). Electromyography excluded any evidence of neuromuscular junction dysfunction, although myopathic features were noted. A lower limb MRI in 2022 demonstrated a pattern of muscle involvement supportive of IBM (Fig. 2) (5). Our neuropathology team reviewed muscle histology previously obtained in 2017; noting features suggestive of IBM (Table I). Previous treatment with intravenous immunoglobulin and prednisolone provided no benefit.

Facial onset IBM with predominant bulbar and respiratory involvement

Case 3

A woman of Pakistani origin was referred to our centre in 2019 aged 63, after having been under her local neu-

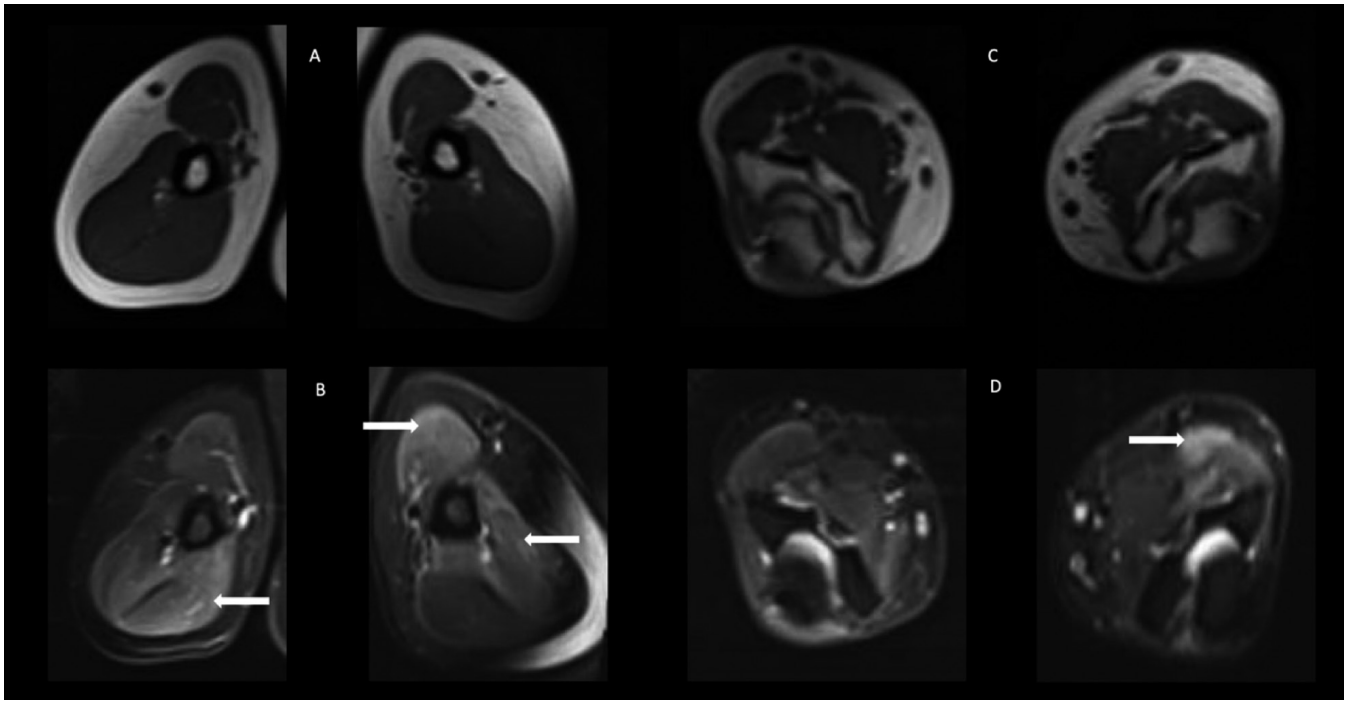

Fig. 1. Upper limb MRI of case 1 in 2020.
(**A-B**) show T1 and T2 STIR sequences of the upper arm. There is evidence of hyperintensity in right triceps, left biceps and lateral aspect of left triceps, see arrows (**B**). (**C-D**) show T1 and T2 STIR sequences at the elbow, there is swelling at left brachioradialis, see arrow (**D**).

rology team for many years. She had a background of hepatitis C, hepatitis B and lichen planus. Since 2014 she developed a progressive facial diplegia with Bell's phenomena. The patient was noted to have a striking macroglossia during this period. In 2017 she underwent a mucosal biopsy of a lichenoid patch on her tongue, confirming lichenoid inflammation. Although no muscle was sampled, histology helped exclude amyloidosis.

She developed worsening orthopnoea in 2015. At the end of 2015 she was hospitalised in Pakistan with pneumonia and type 2 respiratory failure. She was started on NIV, subsequently becoming NIV-dependent overnight. Ultrasound studies revealed evidence of left diaphragmatic weakness. Shortly after this admission she noted difficulty with swallowing.

In 2019 she was intensively re-investigated at our centre. At this stage she needed a stick to walk and had difficulty picking up small objects. On examination she had marked facial diplegia and macroglossia (Fig. 3). There was wasting in right quadriceps and posterior calf muscles. Long finger flexion weakness was the most striking limb deficit (Table II). Her swallow had markedly deteriorated. Videofluoroscopy demonstrated significant oropharyngeal dysphagia and impaired cricopharynx opening. Despite the offer for a percutaneous endoscopically inserted gastrostomy (PEG), she declined alternative feeding routes. Her CK was mildly raised at 429. Blood screening was unremarkable apart from evidence of previous hepatitis B and C infections.

A quadriceps biopsy was performed, with the subsequent histology supporting the diagnosis of IBM (Table II). No limb imaging could be performed due to her inability to lie flat.

Case 4

A 67-year-old woman was referred to our neuroscience centre in 2016. At the age of 60, she had difficulty carrying heavy items. At the same she noticed inappropriate closure of her eyelids and her mouth was progressively 'drooping'. This was coupled with impaired chewing and mild dysphagia. During this period her dentist had commented on her tongue appearing enlarged. Her walking declined over the next seven years.

During her most recent review in 2022 she had severe facial diplegia (Fig. 3). There was evidence of macroglossia, tongue deviation, weak tongue movements and nasal speech (see Table II for limb examination). Videofluoroscopy revealed oropharyngeal dysphagia with no contraction seen in the posterior pharynx, and upper oesophageal sphincter (UES) relaxation was impaired. The patient declined feeding via a PEG. She was also extensively investigated for alternative diagnoses (Table II).

She developed marked orthopnoea in 2020, after years of exertional breathlessness. She was started on overnight NIV since 2021 after being noted to have type 2 respiratory failure. In 2022, her FVC was 55% of that predicted and sleep studies still demonstrated evidence of nocturnal hypoventilation.

Muscle histology obtained in 2015 was indicative of IBM (Table II). The patient had lower limb MRI (Fig. 4); the pattern of muscle involvement was supportive of IBM (5).

Case 5

A 56-year-old female presented to our centre in 2021. She first noticed weakness of the mouth aged 40, noting drib-

Table I. Summary of young-onset inclusion body myositis cases.

Case	Age at onset	Gender	Atypical features	Limb MRC grading for muscle strength and key findings			Biopsy site and key histology findings	Other investigations
1	31	M	Young-onset, arthralgia, limited weakness at onset with raised CK, early proximal lower limb involvement, early triceps changes on MRI, features of connective tissue disorder	**Upper Limb**	Right	Left	Right triceps (2020)	Elevated CK – 800 IU/L (2021)
				Shoulder abduction	5	5		
				Elbow extension	5	5	Endomysial infiltration: Present	Myositis-specific antibody screen negative
				Elbow flexion	5	5		
				Wrist Flexion	5	5	Invasion of non-necrotic fibres:	ANA, Ku and PM/Scl antibody positivity
				Wrist Extension	5	5	Present	
				Long finger flexion *(weakness only in 4th and 5th digits)*	4	4	P62: Present	Raised IgG and IgA Reduced complement
				Abductor pollicis brevis	4-	4-	MHC 1 upregulation: Present	CT Thorax: splenomegaly
				Lower Limb	Right	Left	Rimmed vacuoles: Present	
				Hip Flexion	4+	4+		
				Hip Extension	5	5	Excessive COX negative/deficient	
				Knee Flexion	5	5	fibres: Present	
				Knee Extension	5	5		
				Dorsiflexion	5	5		
				Plantarflexion	5	5		
2	31	F	Young-onset, calf pain, prominent bilateral facial weakness	**Upper Limb**	Right	Left	Right quadriceps (2017)	Elevated CK – 144 IU/L (2022)
				Shoulder abduction	5	5	Endomysial infiltration: Present	Myositis-specific antibody screen negative
				Elbow extension	4+	4		
				Elbow flexion	3	3-	Invasion of non-necrotic fibres:	Borderline AChR antibody positivity
				Wrist Flexion	3	3	Present	
				Wrist Extension	4	4		MUSK antibody negative
				Long finger flexion	2	0	P62: Present	
								FSHD genetic testing negative
				Lower Limb	Right	Left	MHC 1 upregulation: Present	Myofibrillar myopathy genetic testing negative
				Hip Flexion	4+	5		
				Hip Extension	5	5	Rimmed vacuoles: Present	100000 genome – Nil variant of concern
				Knee Flexion	4	5		
				Knee Extension	3	4-	Excessive COX negative/deficient	
				Dorsiflexion	4+	5	fibres: Present	Pompe's screening negative
				Plantarflexion	4	4+		Plasma Carnitine profile - normal

AChR: acetylcholine receptor; COX: cyclooxygenase; CK: creatinine kinase; F: female; FSHD: facioscapulohumeral dystrophy; M: male; MHC: major histocompatibility complex; MRC: medical research council; STIR: Short Tau Inversion Recovery; P62: p62 protein or sequestosome 1.

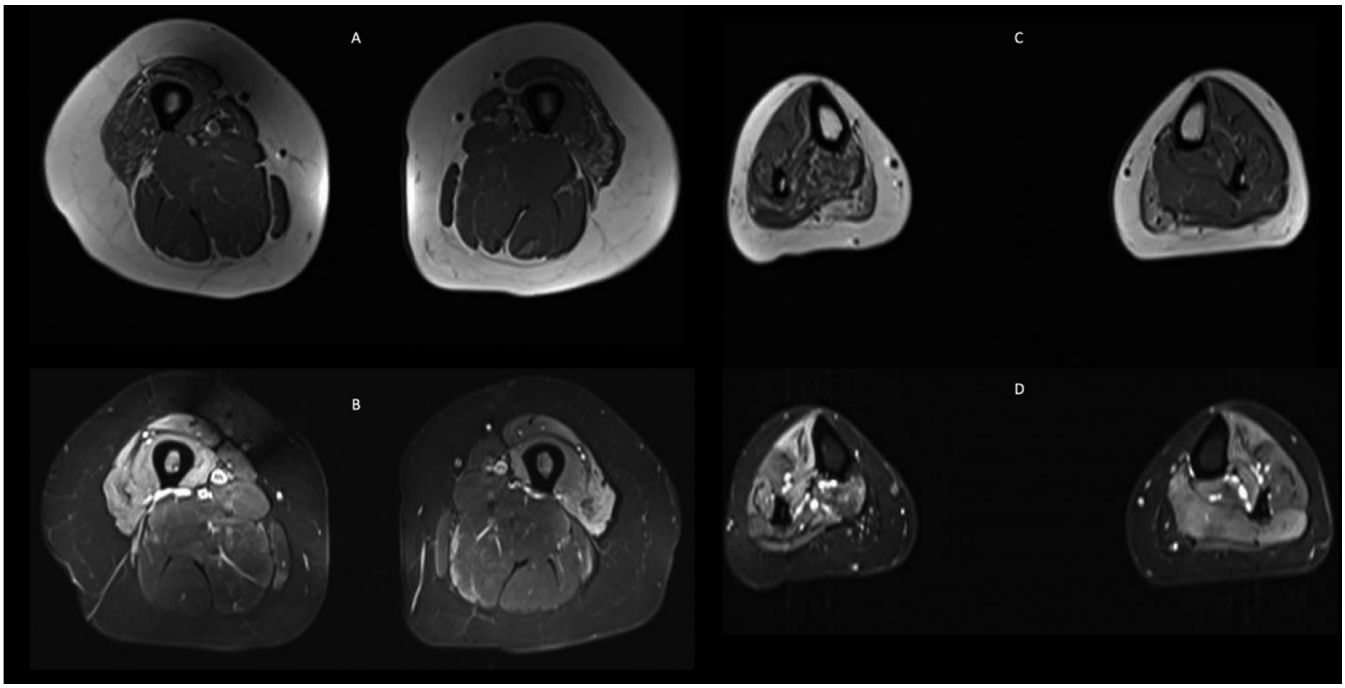

Fig. 2. Lower limb MRI of case 2 in 2022.
(**A-B**) show T1 and T2 STIR sequences of the thighs. There is evidence of fat infiltration (T1 hyperintensity), atrophy and oedema (STIR hyperintensity) of the quadriceps muscle bilaterally. (**C-D**) show T1 and T2 STIR sequences of the calves. There is there is fat infiltration and atrophy in the calves, the most severe involvement is seen in the medial gastrocnemius on both sides with additional patchy oedema most marked in right tibialis anterior.

Table II. Summary of cases with facial weakness at onset with severe dysphagia, bulbar weakness, tongue involvement and respiratory compromise as predominate features.

Case	Age at onset	Gender	Atypical features	Limb MRC grading for muscle strength and key findings			Biopsy site and key histology findings	Other investigations
3	58	F	Facial diplegia at presentation, macroglossia, early bulbar issues including dysphagia and mild dysarthria, early respiratory failure requiring NIV	**Upper Limb**	Right	Left	Left quadriceps (2019)	Elevated CK – 429 IU/L (2019)
				Shoulder abduction	4+	4		
				Elbow extension	4+	4	Endomysial infiltration: Present	Myositis-specific antibody screen negative
				Elbow flexion	4+	4		
				Wrist Flexion	4	4-	Invasion of non-necrotic fibres:	ENA negative
				Wrist Extension	4+	4	Present	Positive serology for Hep B and C
				Long finger flexion	3	0		
				Abductor pollicis brevis	4+	4+	P62: Present	
								FSHD genetic testing negative
				Lower Limb	Right	Left	MHC 1 upregulation: Present	
				Hip Flexion	4+	4		Pompe's screening negative
				Hip Extension	5	5	Rimmed vacuoles: Present	Plasma Carnitine profile- unremarkable
				Knee Flexion	4+	4+		
				Knee Extension	4	4	Excessive COX negative/deficient	Long fatty acid profile – normal
				Dorsiflexion	5	4+	fibres: Present	
				Plantarflexion	3	3		
4	60	F	Facial diplegia at presentation, macroglossia, early bulbar issues including dysphagia and dysarthria, respiratory failure requiring NIV	**Upper Limb**	Right	Left	Left quadriceps (2015)	Elevated CK – 276 IU/L (2022)
				Shoulder abduction	4	4-		
				Elbow extension	3+	3+	Endomysial infiltration: Present	Myositis-specific antibody screen negative
				Elbow flexion	4	4		
				Wrist Flexion	3-	3-	Invasion of non-necrotic fibres:	
				Wrist Extension	4	4-	Present	FSHD genetic testing negative
				Long finger flexion	1	1		Mitochondrial testing: whole genome NGS and 3 common mutations negative
				Abductor pollicis brevis	4-	4-	P62: staining not performed	
				Lower Limb	Right	Left	MHC 1 upregulation: Present	Myotonic dystrophy type 1 & 2 genetic testing negative
				Hip Flexion	4+	4		
				Hip Extension	5-	5-	Rimmed vacuoles: Present	
				Knee Flexion	5-	4-		
				Knee Extension	5-	4-	Excessive COX negative/deficient	
				Dorsiflexion	5	4	fibres: Present	
				Plantarflexion	5	5		
5	40	F	Facial diplegia at presentation, early bulbar issues including dysphagia and dysarthria, respiratory failure requiring NIV	**Upper Limb**	Right	Left	Left quadriceps (2010)	Elevated CK – 258 IU/L (2022)
				Shoulder abduction	2	0		
				Elbow extension	4	3	Endomysial infiltration: Present	FSHD genetic testing negative
				Elbow flexion	4	3		100000 genome – Nil variant of concern
				Wrist Flexion	4	3	Invasion of non-necrotic fibres:	
				Wrist Extension	3	2	Not seen	
				Long finger flexion	3	0		
				(Left medial fingers affected)			P62: staining not performed	
				Abductor pollicis brevis	5	5		
							MHC 1 upregulation: Present	
				Lower Limb	Right	Left		
				Hip Flexion	5	4-	Rimmed vacuoles: Nil seen	
				Hip Extension	3	4		
				Knee Flexion	4	3	Excessive COX negative/deficient	
				Knee Extension	2	1	fibres: Present	
				Dorsiflexion	5	5		
				Plantarflexion	5	5		

COX: cyclooxygenase; CK: creatinine kinase; F: female; FSHD: facioscapulohumeral dystrophy; MHC: major histocompatibility complex; M: male; MRC: grading medical research council; NGS: next generation sequencing; P62: p62 protein or sequestosome 1.

bling from the mouth and difficulty flexing her left index finger. Her facial weakness progressed to become complete, and she required two face lifts. She had dysarthria and dysphagia for more than a decade. Her swallow was very limited and required feeding via a PEG. The patient needed a rolling frame to mobilise.

During her most recent examination in 2022, she was noted to have severe facial diplegia and tongue wasting (see Table II for limb examination). Her respiratory function has declined over the years, and she is unable to lie supine. Her sitting FVC was 22% of predicted in 2022 and had required NIV overnight since 2016.

All her blood tests and genetic screening were unremarkable. Previous screening via the 100,000-genome project revealed no pathogenic variants. In 2010 she had a biopsy which showed evidence of inflammation and excessive COX negative fibres (Table II).

Given her issues with lying supine she underwent a lower limb CT; this showed extensive wasting of the anterior thigh muscles and was supportive of IBM (Fig. 5).

Discussion

There are rare reports of patients developing IBM in their thirties or younger, often in the context of immune dysfunction (6-10). When reflecting on our series, case 1 had non-specific features supportive of an autoimmune (undifferentiated) connective tissue disorder namely Raynaud's phenomenon, arthralgia, raised immunoglobulins, reduced complement, positive autoimmune antibodies and splenomegaly. Case 2 had a background of coeliac disease and non-specific acetylcholine receptor antibody positivity (with no

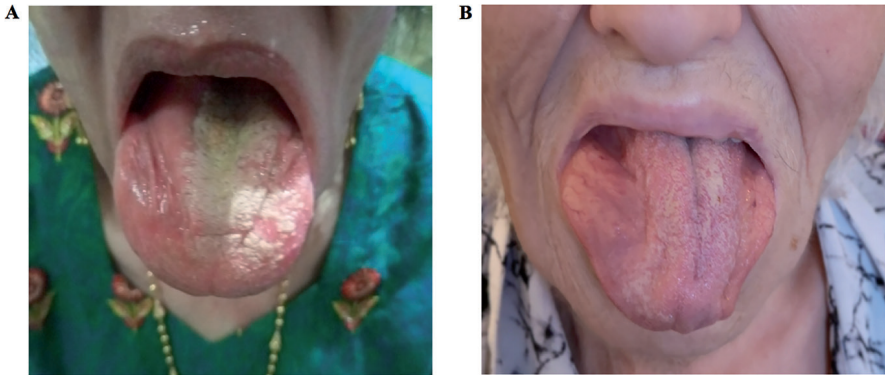

Fig. 3. Clinical evidence of macroglossia.
A: Photograph of tongue from patient in case 3. **B**: Photograph of tongue from patient in case 4.

clinical or electrophysiological correlates), again demonstrating a predilection towards autoimmunity. Clerici *et al*. describe IBM in a man with symptoms since his early thirties, in the context of longstanding rheumatoid arthritis and autoimmune thyroiditis (7). This report again supports an association between young-onset IBM and coexisting autoimmune disease. The authors report regular IVIG improved his symptoms and stabilised muscle strength. T-LGLL has been associated with IBM and other autoimmune diseases (6, 11, 12). T-cells in IBM share similar characteristics to T-LGLL; with the potential for pathogenicity and resisting conventional immunosuppression (11, 13). Importantly, Limaye *et al*. describe a case of young-onset IBM in a 31-year-old woman with a background of both T-LGLL and Sjögren's syndrome (6). She was treated with two courses of rituximab for exacerbations which provided some clinical improvement but did not prevent progression. Although T-LGLL was excluded in case 1, these observations provide a rationale to screen for T-LGLL in younger patients. HIV infection has been associated with IBM in younger individuals and should be excluded in the diagnostic work up (1). A series of reports have described HIV patients in their thirties developing IBM (14, 15). Lloyd *et al*. describe a cohort of 11 HIV patients, displaying overlapping features of IBM and polymyositis, with three cases aged between 28-32 (16).

Despite the potential support for the association of immune dysfunction with young-onset IBM, this observation is not universally seen (8, 9). Walsh *et al*. presented a case of rapidly progressing IBM in a 31-year-old woman, with no overt features of autoimmunity (8). The authors describe progressive limb (both proximal and distal) weakness and dysphagia. The patient became wheelchair bound within a year. She did not respond to oral steroids or IVIG. Furthermore, both young-onset cases in our series also did not respond to immunosuppression or immunomodulation. Clearly the relationship between immune dysfunction and young-onset IBM needs further investigation.

The second subset described in this series, is prominent facial weakness at onset in middle aged women, followed by a clinical picture dominated by marked dysphagia, bulbar involvement and respiratory failure requiring

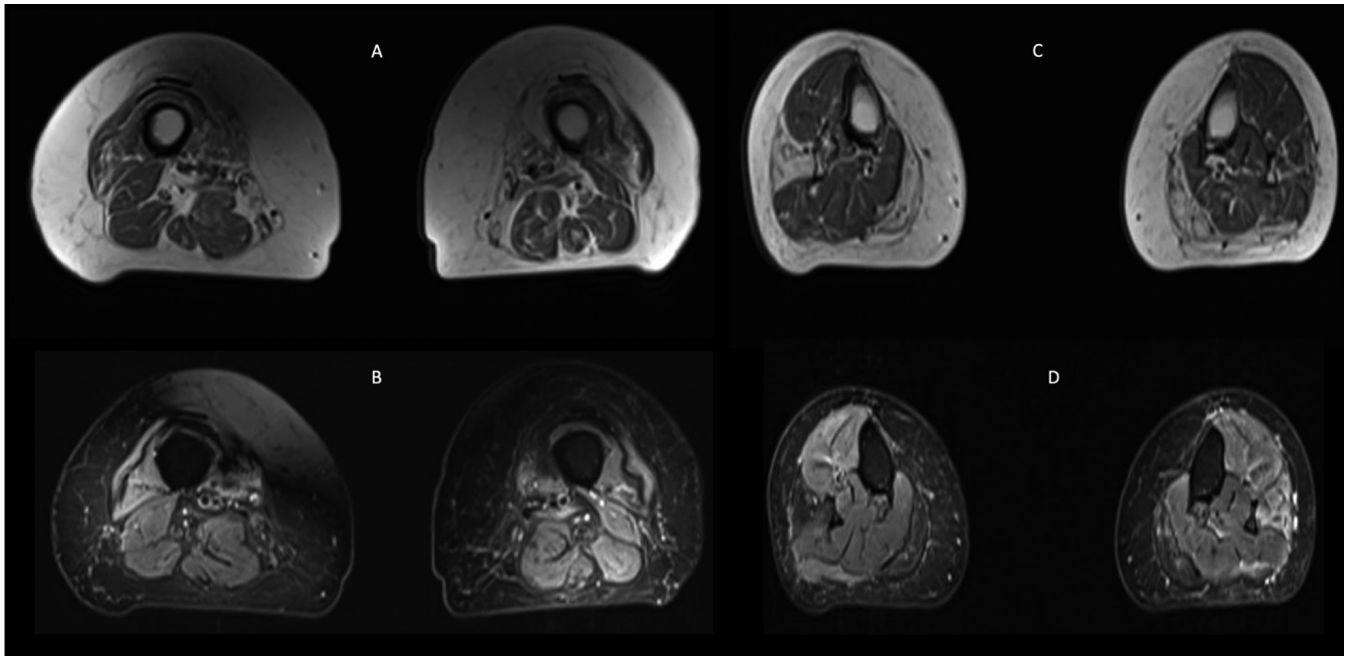

Fig. 4. Lower limb MRI of case 4 in 2016.
(**A-B**) show T1 and T2 STIR sequences of the thighs. There is evidence of fat infiltration in anterior compartments of thigh bilaterally. (**C-D**) show T1 and T2 STIR sequences of the calves. There is fat infiltration in the calves with almost complete fat replacement of medial gastrocnemius and severe involvement of lateral gastrocnemius on the left and peroneus longus on the right. There is patchy oedema especially in right tibialis anterior and left peroneus longus.

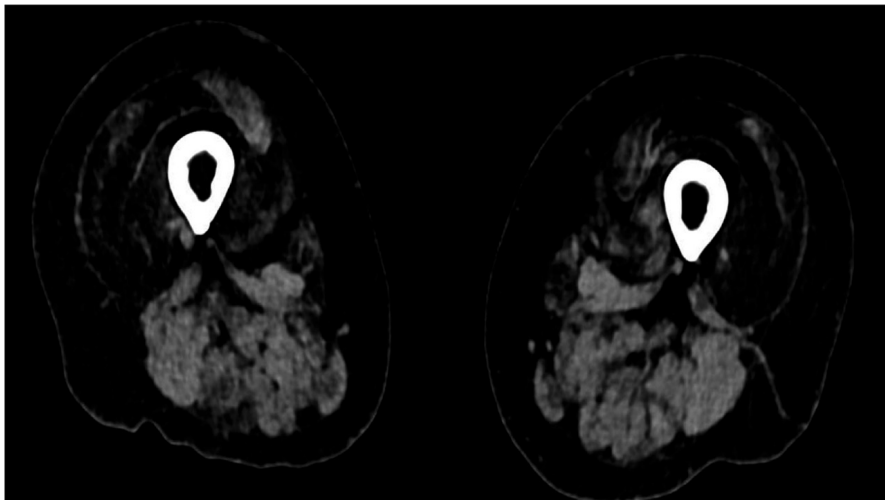

Fig. 5. Lower limb CT of case 5 in 2022.
Marked hypoattenuation in the anterior compartment muscles of the thigh in both legs, indicative of muscle atrophy.

NIV. Facial diplegia as an initial presenting feature in IBM has rarely been described within the literature (10, 17, 18). All these cases have been reported in female patients. However early bilateral facial weakness with the distinctive features seen in this series has not been previously characterised. Ghosh *et al*. describe a 58-year-old woman who developed marked facial diplegia at presentation but did not develop quadriceps or finger flexor weakness after six years (17). However, a biceps biopsy demonstrated histological features of IBM in this case. Cummins *et al*. describe a 68-year-old woman with facial diplegia as the presenting feature. This patient did develop severe finger flexor weakness and muscle histology demonstrated histological features of IBM (18). Alamr *et al*. conducted a cohort study on a population of 357 IBM patients presenting to the Mayo Clinic between 2015-2020, of which 50 patients were classified as 'atypical' based on presenting symptoms (10). The vast majority of atypical cases (78%), eventually went on to meet European Neuromuscular Centre criteria for IBM. The authors further subdivided these patients into seven subgroups based on presenting clinical features including facial weakness, and dysphagia. They also describe a subtype presenting with a raised CK, but no or minimal muscle symptoms, similar to what we observed in case 1 (10). Dysphagia accounted for 50% of their atypical cohort (10). Facial diplegia was seen in two of their atypical cases. These two cases had bulbar weakness and oropharyngeal dysphagia at diagnosis. Again, dysphagia and bulbar dysfunction was noted early on in cases 3-5. Dysphagia is sometimes overlooked in IBM, but comes with significant morbidity and risk of mortality from complications such as aspiration pneumonia (1). Observations suggest that dysphagia may also be more common in female IBM patients (10, 19). Videofluoroscopy findings that are often reported in IBM include impaired pharyngeal propulsion, cricopharyngeal dysfunction and the presence of a cricopharyngeal bar (3, 19-22). There is also suggestion of impaired UES opening in IBM (20). More research into the structural changes propagating dysphagia in IBM is needed. Although some studies suggest a role for IVIG, the most appropriate treatment for dysphagia in IBM is unclear (23). Our series highlights that bulbar weakness in IBM can be severe enough to require alternative feeding routes. All three cases with this phenotype required NIV. Case 3 developed respiratory failure requiring ventilation within 1-2 years of symptom onset. Facial diplegia may also provide specific challenges when delivering NIV via a mask, due to difficulties with obtaining an effective seal. Respiratory compromise in IBM is likely to be underreported, as many patients have asymptomatic or subclinical involvement (24). Respiratory failure as a presenting feature in IBM has infrequently been reported (19, 25-29). A few cases of IBM have described severe respiratory dysfunction on presentation requiring intubation and intensive care admission (27-29). Although respiratory failure is a leading cause of death in IBM, the mechanisms behind respiratory involvement require better characterisation (30). In case 3 we were able to demonstrate ultrasound evidence of diaphragmatic weakness. It is likely that severe respiratory failure in IBM to the extent of what was observed in this series is predominantly due to diaphragmatic weakness; selected reports have demonstrated concrete evidence of diaphragm involvement (26, 31, 32). Macroglossia was noted in two cases belonging to the second phenotype outlined in our series. A mucosal biopsy was performed in case 3 and helped exclude amyloidosis. There are only two formal reports of macroglossia in IBM (33, 34). Similarly to our series, both reports describe facial weakness at presentation and dysphagia. Ganesh *et al*. presented a case series of three IBM patients with macroglossia at presentation (34). These patients did not respond to steroids or IVIG. Yamasaki *et al*. describe macroglossia in a 77-year-old woman diagnosed with IBM and Sjögren's syndrome (33). A tongue MRI demonstrated muscle hypertrophy and fatty deposition in this patient. Treatment with pulsed prednisolone and IVIG, followed by low dose prednisolone improved her ambulation and neck weakness. However, her dysphagia progressed, and she required a PEG (33). Tongue muscle histology described in both reports demonstrated features supportive of IBM (33, 34).

Conclusions

This case series has highlighted the importance of considering IBM in differential diagnosis when investigating myopathy in younger patients. Awareness that IBM can rarely present in patients aged in their thirties or younger is important. These patients may not present with a classical clinical picture. Younger patients should be screened

for T-LGLL along with HIV. The role of more conventional immunosuppression in young-onset IBM patients is unclear at this stage.

The second pattern described is early facial diplegia followed by marked bulbar impairment and respiratory failure in middle-aged females. To our knowledge this is the first formal characterisation of this clinical phenotype. This is the second manuscript to formally describe macroglossia as presenting feature in IBM. Closer evaluation of IBM natural history studies may help define this subset. From a clinical perspective this is important as these patients may need closer follow up, and early involvement from specialties such as gastroenterology and respiratory.

References

1. GREENBERG SA: Inclusion body myositis: clinical features and pathogenesis. *Nat Rev Rheumatol* 2019; 15(5): 257-72. https://doi.org/10.1038/s41584-019-0186-x
2. SNEDDEN AM, KELLETT KAB, LILLEKER JB, HOOPER NM, CHINOY H: The role of protein aggregation in the pathogenesis of inclusion body myositis. *Clin Exp Rheumatol* 2022; 40(2): 414-24. https://doi.org/10.55563/clinexprheumatol/pp0oso
3. CARDELLI C, ZANFRAMUNDO G, COMETI L *et al*.: Idiopathic inflammatory myopathies: one year in review 2021. *Clin Exp Rheumatol* 2022; 40(2): 199-209. https://doi.org/10.55563/clinexprheumatol/vskjxi
4. SALAM S, DIMACHKIE MM, HANNA MG, MACHADO PM: Diagnostic and prognostic value of anti-cN1A antibodies in inclusion body myositis. *Clin Exp Rheumatol* 2022; 40(2): 384-93. https://doi.org/10.55563/clinexprheumatol/r625rm
5. ALFANO LN, FOCHT GARAND KL, MALANDRAKI GA *et al*.: Measuring change in inclusion body myositis: clinical assessments versus imaging. *Clin Exp Rheumatol* 2022; 40(2): 404-13. https://doi.org/10.55563/clinexprheumatol/0q2voe
6. LIMAYE VS, CASH K, SMITH C *et al*.: Inclusion-body myositis and primary Sjögren syndrome: mechanisms for shared etiologies. *Muscle Nerve* 2020; 61(5): 570-74. https://doi.org/10.1002/mus.26830
7. CLERICI AM, BONO G, DELODOVICI ML *et al*.: A rare association of early-onset inclusion body myositis, rheumatoid arthritis and autoimmune thyroiditis: a case report and literature review. *Funct Neurol* 2013; 28(2): 127-32. https://doi.org/10.11138/FNeur/2013.28.2.127
8. WALSH A, RAKOCEVIC G: Early onset and fulminant course of sporadic inclusion body myositis (sIBM): a case report (P3.291). *Neurology* 2014; 82(10 Suppl.): P3.291.
9. DEL BIGIO MR, JAY V: Inclusion body myositis with abundant ring fibers. *Acta Neuropathol* 1992; 85(1): 105-10. https://doi.org/10.1007/BF00304640
10. ALAMR M, PINTO MV, NADDAF E: Atypical presentations of inclusion body myositis: Clinical characteristics and long-term outcomes. *Muscle Nerve* 2022; 66(6): 686-93. https://doi.org/10.1002/mus.27716
11. GREENBERG SA, PINKUS JL, AMATO AA, KRISTENSEN T, DORFMAN DM: Association of inclusion body myositis with T cell large granular lymphocytic leukaemia. *Brain* 2016; 139(5): 1348-60. https://doi.org/10.1093/brain/aww024
12. GREENBERG SA, PINKUS JL, KONG SW *et al*.: Highly differentiated cytotoxic T cells in inclusion body myositis. *Brain* 2019; 142(9): 2590-604. https://doi.org/10.1093/brain/awz207
13. GOYAL NA, COULIS G, DUARTE J *et al*.: Immunophenotyping of inclusion body myositis blood T and NK cells. *Neurology* 2022; 98(13): e1374-e83. https://doi.org/10.1212/WNL.0000000000200013
14. CUPLER EJ, LEON-MONZON M, MILLER J *et al*.: Inclusion body myositis in HIV-1 and HTLV-1 infected patients. *Brain* 1996; 119 (Pt 6): 1887-93. https://doi.org/10.1093/brain/119.6.1887
15. HINIKER A, DANIELS BH, MARGETA M: T-Cell-mediated inflammatory myopathies in HIV-positive individuals: a histologic study of 19 cases. *J Neuropathol Exp Neurol* 2016; 75(3): 239-45. https://doi.org/10.1093/jnen/nlv023
16. LLOYD TE, PINAL-FERNANDEZ I, MICHELLE EH *et al*.: Overlapping features of polymyositis and inclusion body myositis in HIV-infected patients. *Neurology* 2017; 88(15): 1454-60. https://doi.org/10.1212/wnl.0000000000003821
17. GHOSH PS, LAUGHLIN RS, ENGEL AG: Inclusion-body myositis presenting with facial diplegia. *Muscle Nerve* 2014; 49(2): 287-9. https://doi.org/10.1002/mus.24060
18. CUMMINS G, O'DONOVAN D, MOLYNEUX A, STACPOOLE S: Facial diplegia as the presenting symptom of inclusion body myositis. *Muscle Nerve* 2019; 60(2): E14-E16. https://doi.org/10.1002/mus.26514
19. OH TH, BRUMFIELD KA, HOSKIN TL, KASPERBAUER JL, BASFORD JR: Dysphagia in inclusion body myositis: clinical features, management, and clinical outcome. *Am J Phys Med Rehabil* 2008; 87(11): 883-9. https://doi.org/10.1097/PHM.0b013e31818a50e2
20. MURATA KY, KOUDA K, TAJIMA F, KONDO T: A dysphagia study in patients with sporadic inclusion body myositis (s-IBM). *Neurol Sci* 2012; 33(4): 765-70. https://doi.org/10.1007/s10072-011-0814-y
21. OLTHOFF A, CARSTENS PO, ZHANG S *et al*.: Evaluation of dysphagia by novel real-time MRI. *Neurology* 2016; 87(20): 2132-8. https://doi.org/10.1212/WNL.0000000000003337
22. OH TH, BRUMFIELD KA, HOSKIN TL *et al*.: Dysphagia in inflammatory myopathy: clinical characteristics, treatment strategies, and outcome in 62 patients. *Mayo Clin Proc* 2007; 82(4): 441-7. https://doi.org/10.4065/82.4.441
23. JONES K, PITCEATHLY RD, ROSE MR *et al*.: Interventions for dysphagia in long-term, progressive muscle disease. *Cochrane Database Syst Rev* 2016; 2(2): CD004303. https://doi.org/10.1002/14651858.CD004303.pub4
24. RODRIGUEZ CRUZ PM, NEEDHAM M, HOLLINGSWORTH P, MASTAGLIA FL, HILLMAN DR: Sleep disordered breathing and subclinical impairment of respiratory function are common in sporadic inclusion body myositis. *Neuromuscul Disord* 2014; 24(12): 1036-41. https://doi.org/10.1016/j.nmd.2014.08.003
25. LELIEVRE MH, STIENNON, O, BOTEZ, SA, DUBE, BP: A 63-year-old man presents with slowly progressive dyspnea on exertion and lower extremity muscle weakness. *Chest* 2018; 154(3): e83-e86. https://doi.org/10.1016/j.chest.2018.02.004
26. VOERMANS NC, VANEKER M, HENGSTMAN, GJ *et al*.: Primary respiratory failure in inclusion body myositis. *Neurology* 2004; 63(11): 2191-2. https://doi.org/10.1212/01.wnl.0000145834.17020.86
27. COHEN R, LIPPER S, DANTZKER DR: Inclusion body myositis as a cause of respiratory failure. *Chest* 1993; 104(3): 975-7. https://doi.org/https://doi.org/10.1378/chest.104.3.975
28. DARDIS C, ANTEZANA A, TANJI K, MACCABEE PJ: Inclusion body myositis: a case presenting with respiratory failure and autopsy findings leading to the hypothesis of a paraneoplastic cause. *Am J Case Rep* 2017; 18: 700-6. https://doi.org/10.12659/ajcr.903566
29. JETHAVA A, ALI S, DASANU CA: Primary respiratory failure due to inclusion body myositis: think outside the box. *Conn Med* 2013; 77(3): 155-8.
30. COX FM, TITULAER MJ, SONT JK *et al*.: A 12-year follow-up in sporadic inclusion body myositis: an end stage with major disabilities. *Brain* 2011; 134(Pt 11): 3167-75. https://doi.org/10.1093/brain/awr217
31. MARTIN SE, GONDIM DD, HATTAB EM: Inclusion body myositis involving the diaphragm: report of a pathologically confirmed case. *Neurol India* 2014; 62(1): 66-7. https://doi.org/10.4103/0028-3886.128313
32. LELIÈVRE MH, HUDSON M, BOTEZ SA, DUBÉ BP: Determinants and functional impacts of diaphragmatic involvement in patients with inclusion body myositis. *Muscle Nerve* 2021; 63(4): 497-505. https://doi.org/10.1002/mus.27170
33. YAMASAKI Y, MUKAINO A, YAMASHITA S *et al*.: Macroglossia in rapidly progressive inclusion body myositis. *Neuropathology* 2022 Nov 8. https://doi.org/10.1111/neup.12879
34. GANESH V, SEYEDSADJADI R, DAVID W, AMATO A: Case series of inclusion body myositis presenting with macroglossia. *Muscle Nerve* 2019; 60: S17.