Acta Myologica • 2019; XXXVIII: p. 37-40

CASE REPORTS

Subacute inflammatory myopathy associated with papillary cancer of the thyroid gland

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Inflammatory myopathies comprise a group of rare autoimmune muscle diseases characterized by a variable degree of muscle weakness, elevated creatine kinase levels and necrotic fibres associated with invading inflammatory cells at histologic examination. Although there are several reports about their relationship with malignancy, association with papillary cancer of the thyroid gland is extremely rare. We present a case of a female patientdiagnosed withinflammatory myopathy and apapillary cancer of the thyroid gland, with a remarkable clinical improvement after thyroid cancer surgery and radioactive iodine treatment, supporting a correlation between the two conditions.

Key words: inflammatory myopathy, polymyositis, dermatomyositis, thyroid gland papillary cancer

Introduction

Inflammatory myopathies (IM), like as polymyositis (PM), dermatomyositis (DM), inclusion body myositis and immune-mediated necrotizing myopathy,are a group of idiopathic inflammatory muscle diseases characterized by a variable degree of muscle weakness and elevated creatine kinase levels (CK) (1). Diagnosis is usually based on a combination of clinical, laboratory and muscle biopsy findings. Although DM and PM may be associated with neoplastic conditions, patients with DM have a higher risk of associated malignancy, namely ofcolorectal, breast, lung, ovarian and pancreatic origin (6-60%)(2) but previous nationwide studies have not had sufficient cases to test the association between myositis and specific cancer types. Our aim was to investigate the risk of specific cancer types in individuals with dermatomyositis and polymyositis. Methods: We did a pooled analysis of published national data from Sweden, Denmark, and Finland. All patients with dermatomyositis and polymyositis (≥ 15 years old. The association of IM with malignancyof the thyroid gland is extremely rare (3, 4). We report a patient diagnosed with inflammatory myopathy and papillary cancer of the thyroid gland (PCTG), with a remarkable clinical improvement after thyroid cancer surgery, radioactive iodine and immunosuppressive treatment.

Case report

A previously healthy 62-year-old female, with negative family history for neuromuscular disorders, presented a 6-month history of progressive proximal upper and lower limbs muscle weakness,low-tone hypophonia anddysphagia, and weight lossof 10kg. The patient was not able to take care of her daily basic needs and looked emaciated and ill. She could not brush her hair or getting up from a chair without help.There was muscle atrophy of the thighs and the lumbar paraspinal muscles. She walked with a significant waddling gait and hyperlordosiswith the shoulders placed backwards. The patient was not able to get up from the ground (positive Gowers´manoeuver). Manual muscle testing, graded according to the MRC scale, revealed a proximal upper and lower limbs muscle weakness, grade 3, and 4- in the anterior flexion of the head. Myotatic reflexes were absent throughout. Sensory examination was normal and there were novisible fasciculations.

Careful skin examinationshowed no abnormalities on the face, hands or fingers. CK values were slightly elevated (803 UI/L; normal < 180 UI/L), antinuclear antibodies were detected in low titter (1:640) and thyroid hormones values were normal. The myositis-specific antibody anti-Jo-1 and paraneoplastic antibodies were negative.

Electromyography of the upper and lower limbs muscles showed a myopathic pattern (small polyphasic motor unit action potentials with early recruitment), without abnormal spontaneous activity andnormal motor and sen-

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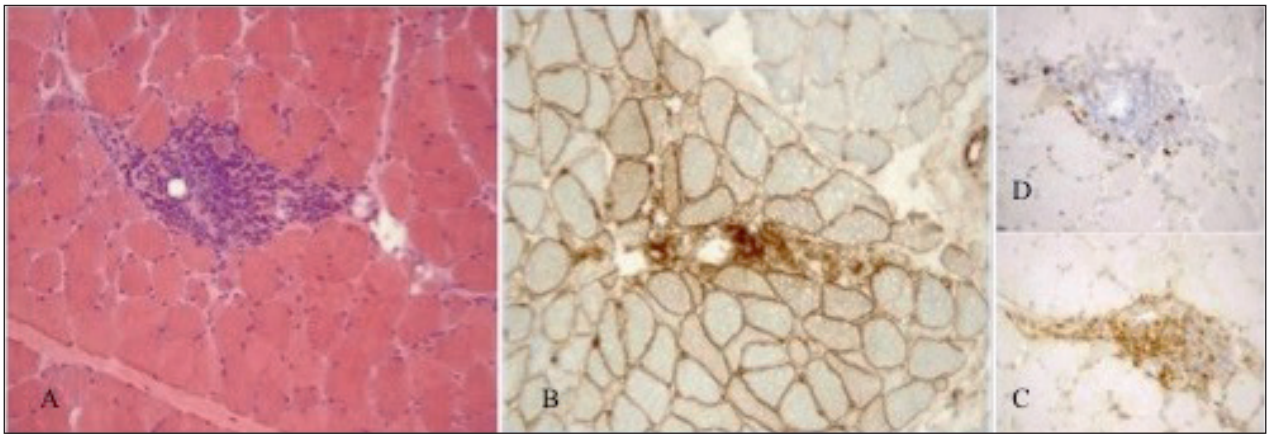

Figure 1. Histological examination of left deltoid muscle biopsy. A) Variability in fibre size and perivascular/perimysial inflammatory infiltration (HE 200x); B) Positive MHC staining;C) CD4+ lymphocytes (400x); D) CD8+ lymphocytes (400x).

sory nerve conduction studies. Histological examination of the left deltoid muscle (Fig. 1) showedfibre necrosis, increased variability of muscle fibre diameter, degeneration with muscle fibre regeneration, and a predominantly perivascular/perimysial inflammatory infiltrate of CD4 + type cells. There were no signs of perifascicular atrophy. Dystrophin was normally expressed with anti-*Dys*1, 2 and 3, as well as dysferlin, sarcoglycans, merosin and α-dystroglycans.Muscle magnetic resonanceimaging (Fig. 2) revealed oedema and fatty infiltration replacing dorsal and lumbar musclesparaspinal. The patient started oral prednisolone (1mg/kg/day) with slight decrease of CK values,but withoutsignificant clinical improvementduring the three following months, which prompted a wider investigation strategy, includinga whole-body PET scan, which identified hypercaptation in the left thyroid lobe. A fine-needle thyroid aspiration biopsy was performed, revealing malignant cells consistent withpapillary carcinoma of the thyroid gland (PCTG). A total thyroidectomy was performed and the patient was started on levothyroxine (0,1mg id), together with a 1mg/kg/day of steroid treatment, with partial clinical improvement of the bulbar function and axial and proximal muscle weakness. Meanwhile, histological studies of the resected thyroid tissue (Fig. 3) identified invasion of two surgical margins by neoplastic cells, compatible with an incomplete removal of the thyroid malignancy. The patient underwent radioactive iodine-131 treatment for 60 days.Three months after radioactive treatments, and under a steroid-tapering regimen to an alternate daily dose of 10 mg,there was a remarkable improvement of her neurological condition, with the patient being fully autonomous in her daily life. There was no muscle weakness in the upper limbs and there was a complete recovery of the bulbar function and cervical muscles strength. The patient was able to get up from a chair without support, and the proximal lower limb muscle strength was graded 4 +. She still walked with hyperlordosis and presented a slight waddling gait.

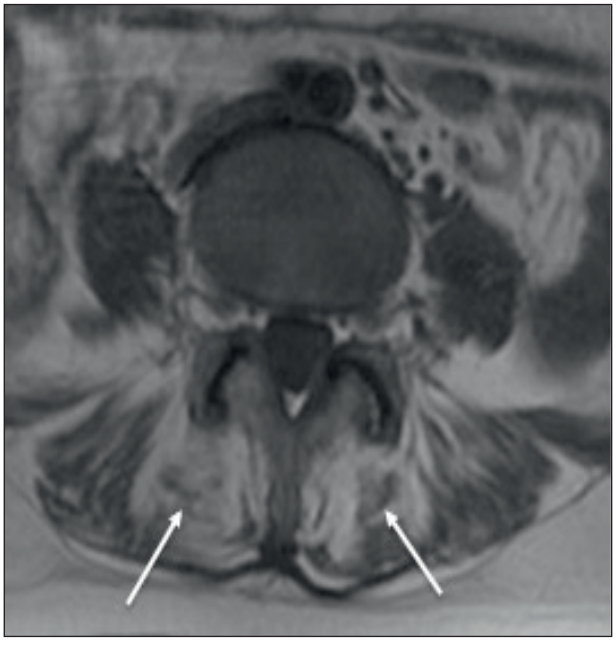

Figure 2. Lumbar paraspinal muscle MRI (T1-weighted sequence): severe atrophy of lumbar paraspinals muscles (white arrow).

Discussion

Inflammatory myopathies (2) but previous nationwide studies have not had sufficient cases to test the association between myositis and specific cancer types. Our

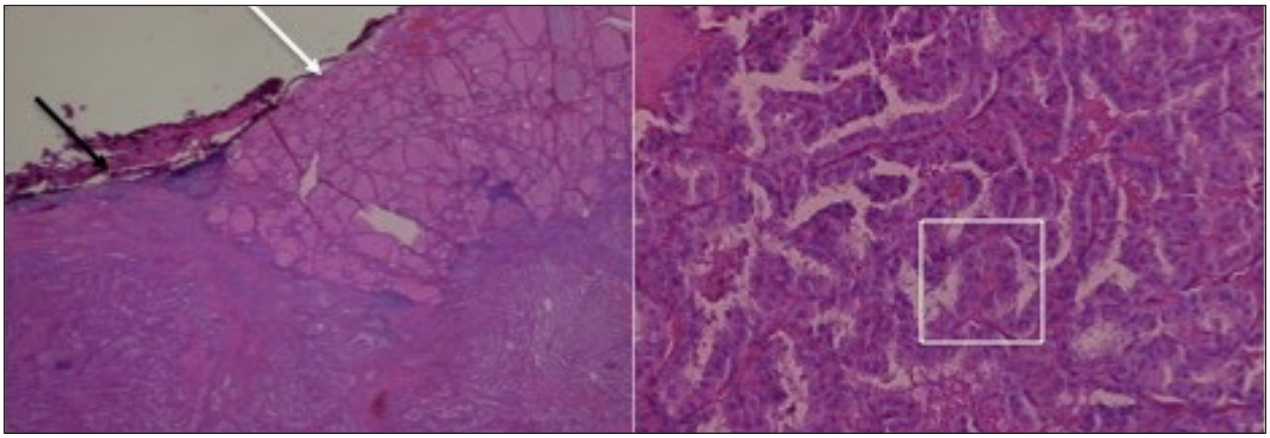

Figure 3. Histological examination of thyroid gland. A) Neoplastic thyroid cells invading the margin of the resected tissue (black arrow) and healthy thyroid cells (white arrow) (HE 100x); B) Thyroid gland neoplastic cells forming papillary structures (white square) (HE 200x).

aim was to investigate the risk of specific cancer types in individuals with dermatomyositis and polymyositis. Methods: We did a pooled analysis of published national data from Sweden, Denmark, and Finland. All patients with dermatomyositis and polymyositis (≥ 15 years old may be associated with malignancy, which can occur previously or after the IM diagnosis.

In the presence of malignancy, creatine kinase values are less elevated than in idiopathic cases, the muscle disease is more protracted and less responsive to treatment (4). Removal of the coexisting malignancy is of paramount importance in improving muscle disease. In case of incomplete removal of the tumour, clinical complete recovery may not occur. In our patient, the improvement of muscle weakness after radioactive iodine-131 treatment highlights the importance of successful tumour treatment and reinforces the causal relationship between malignancy and IM (5).

The incidence of thyroid cancer in US increased from 3.6 per 100,000 in 1973 to 8.7 per 100,000 in 2002, probably due to an increased detection of the subclinical disease and increased diagnostic scrutiny, rather than an increase in the incidence of thyroid cancer (6).

PCTG is a very uncommon solid tumour, and its association with IM is extremely rare, with only a few cases reported in the literature, mainly associated with DM (7).

The majority of patients diagnosed with DM have particular skin changes (heliotrope rash and Gottron papules). These can be subtle and being unnoticed or can occur later in the disease course. However, very occasionally, skin abnormalities are not present (*Dermatomyositis sine dermatitis*) (8).

Histological changes in DM are characterized by infiltration of inflammatory cells, predominantly CD4+, in muscle and skin capillaries (perimysial/perifascicular infiltration) and perifascicular atrophy, which is considered the most relevant histological marker of DM.In PM cases, histological examination typically reveals cellular infiltrates located chiefly within the fascicle, consisting of cytotoxic CD8+, T-cells and macrophages (9).

The muscle biopsy findings of our patient are more in agreement with the histopathological findings of DM. However, the lack of perifascicular atrophy and the remaining clinical and laboratory findings (mainly absence of skin changes and negative anti-J yo-1 antibodies), suggests a non-specific inflammatory myopathy.

In this clinical case, sporadic inclusion body myositis can be ruled out based on clinical presentation and pathological findings, which are quite different from what this patient present, as well as acute necrotizing myopathy, which is a severe acute muscle disease associated with high levels of CK and distinctive pathological findings (10).

In conclusion, papillary carcinoma of thyroid gland is extremely uncommon and very rarely reported in association with inflammatory myopathy and since it is a treatable tumour, it should be considered in every patient with inflammatory myopathy non-responsive or refractory to treatment.

Conflict of interest

The Authors declare to have no conflict of interest.

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How to cite this article: Martins AI, Lages A, Rebelo O, et al. Subacute inflammatory myopathy associated with papillary cancer of the thyroid gland. Acta Myol 2019;38:37-40