A rare case of paraneoplastic myositis associated with neuroendocrine carcinoma of the pancreas

F. Decraene, F. Van De Mierop

Department of Gastroenterology, GZA Sint-Augustinus, Wilrijk, Belgium.

Abstract

Pancreatic cancer is only rarely associated with myopathy. We present a case of a 69-year-old male with recently diagnosed pancreatic cancer, who presented himself with a paraneoplastic myositis of both legs. MRI and EMG contributed to this diagnosis. Treatment was started with high dose corticosteroids followed by urgent laparoscopic pancreaticoduodenectomy. Postoperatively there was a rapid normalisation of the creatinine kinase levels with gradual increase of the muscle strength. The anatomopathology of the biopsy specimen showed a large cell neuroendocrine carcinoma. Paraneoplastic myositis associated with pancreatic cancer may be treated successfully with cancer specific treatment. (Acta gastroenterol. belg., **2022,** 85, **1-3**).

Keywords: pancreatic cancer, myositis, paraneoplastic syndrome, pancreaticoduodenectomy.

Introduction

Inflammatory myopathies, like polymyositis or dermatomyositis, are known to be associated with malignancy. Recently, cancer-associated myositis (CAM) has been defined as a paraneoplastic syndrome due to the anti-tumour immunity that targets similar tumour and regenerating muscle antigens (1). The prognosis of myositis depends on the treatment and prognosis of the underlying malignancy and is unfavourable when there is significant muscle weakness at diagnosis (2). The malignancies most associated with inflammatory myositis are carcinoma of the breast, lung, colorectal, pancreas, ovaria and bladder (3-4).

We report a case of a patient with a large cell neuroendocrine carcinoma (NEC) of the pancreas and an unusual presentation of myositis. Only a few authors have reported myositis as a paraneoplastic syndrome associated with pancreatic adenocarcinoma (5-7). To our knowledge, this is the first report of a CAM associated with a neuroendocrine carcinoma of the pancreas.

Case report

In December 2020 a 69-year-old man presented himself with jaundice, diarrhea, anorexia and weight loss of 10 kg during the past month. His medical history included asthma-COPD overlap syndrome, dyslipidaemia, cataract surgery, familial long QT syndrome and a TIA in 2020. His family history included familial long QT syndrome in his mother and a sister with breast carcinoma. Imaging with CT and MR showed a 54 mass in the processus uncinatus of the pancreas with double duct sign and no evidence of distant metastasis, lymph node involvement or invasion of major blood vessels. Fine needle aspiration was performed during endoscopic ultrasound and immunohistochemistry suggested an adenocarcinoma. Because of obstructive jaundice an endoprosthesis of polyethylene was placed endoscopically in the main bile duct. Surgical resection was foreseen after complete resolution of jaundice and optimalisation of his general condition but two days after the procedure, the patient presented himself with progressive muscle weakness in his legs with severe impairment of his mobility. This was not accompanied with pain, loss of sensation or skin abnormalities.

Laboratory investigation on re-admission revealed a creatinine kinase level of 2443 U/l (reference range 30 -200 U/l); aspartate aminotransferase 373 U/l (reference level < 34 U/l); alanine aminotransferase 287 U/l (reference level < 55 U/l); lactate dehydrogenase 441 U/l (reference range 125-220 U/l). After stenting the total bilirubin level was decreased from 25.6 mg/dl to 12.2 mg/dl (reference range 0.3-1.2 mg/dl). C-reactive protein was 14 mg/l (reference level < 6 mg/l). The patient denied any recent trauma or intramuscular injection. A myositis work up was determined, as shown in Table 1. Magnetic resonance imaging of the upper legs showed diffuse T2 hyperintensity in different muscle compartments, compatible with edema (Fig. 1). Elektromyographic findings revealed serious myogenic degeneration in the proximal extremities with a superponated moderate demyelinating and axonal polyneuropathy in the lower legs. An open muscle biopsy of the vastus lateralis was performed but unfortunately, the biopsy sample didn't contain enough muscle tissue to be admissible for interpretation.

Initially, therapy was started with methylprednisolone 64 mg orally but this was increased to methylprednisolone 1000 mg intravenously because of further exponential increase of the creatinine kinase levels above measurable

Correspondence to: Francesca Decraene, resident gastroenterology, KU Leuven, Herestraat 49, 3000 Leuven, Belgium. Phone: 016 34 59 71.
Email: francesca.decraene@uzleuven.be

Submission date: 21/06/2021
Acceptance date: 03/09/2021

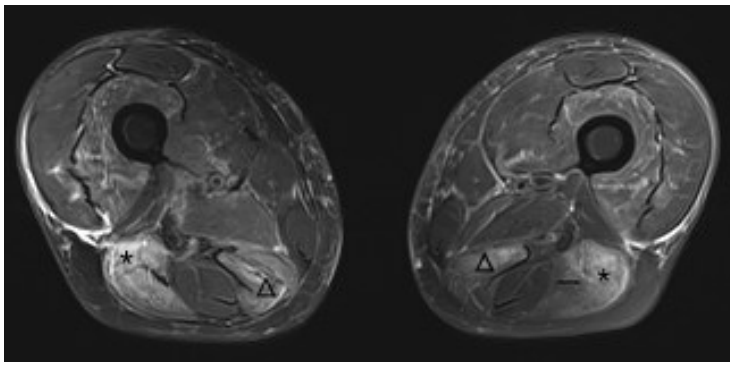

Figure 1. — MRI, axial T2-weighted sequences (fat sat TSE) of both thighs revealed edema in the musculus quadriceps, musculus adductur magnus and the hamstrings, most prominent in the musculus semimembranosus (indicated by Δ) and the musculus biceps femoris (indicated by *).

Table 1. — **Results of the blood tests performed.** The myositis antibody plot tested for specific antibodies (*) who are seen primarily in (dermato)myositis. In addition, we performed a screening of antibodies and viral serology to rule out other autoimmune and infectious diseases.

Test	Result
ANF	Negative
ANCA	Negative
Myositis antibody blot (anti-Jo1, anti-PL7, anti-PL12, anti-EJ-, anti-SRP, antiMi2, anti-MDA5, antiTIF1y, anti-RO52, anti-SAE1, anti-SAE2 en anti-NPX2)*	Negative
IgG4	Normal
Complement C3	Normal
Complement C4	Normal
HIV	Negative
EBV IgG EBNA	Positive
EBV IgM	Negative
Cytomegalo IgG	Negative
Cyomegalo IgM	Negative
Enterovirus antibody	Negative

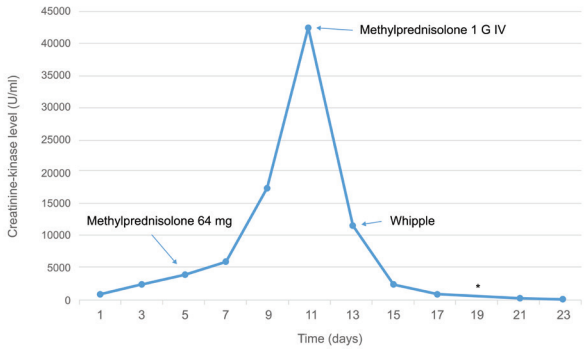

Figure 2. — Evolution of the creatinine kinase level; * no measurement on day 19; IV: intravenously

levels (> 42 670 U/L). This dosage effectively decreased the level to 11 716 U/L. On the day of Christmas Eve, an urgent total laparoscopic pancreaticoduodenectomy (Whipple) with aortacaval lymph node dissection was performed. Pathologic examination revealed a R0 resected large cell neuroendocrine carcinoma of the pancreas. Postoperatively, the dose of glucocorticoids was gradually tapered with complete normalisation of the creatinine kinase level within a week (Fig. 2). After extensive revalidation, adjuvant chemotherapy was started with six cycli of carboplatinum – etoposide. During this adjuvant treatment until June 2021 the patient was doing well. He had regained his mobility and for the time being, there was no evidence of recurrence of his cancer or the myositis.

Discussion

In this case report, the presentation of proximal, symmetrical muscle weakness with rapid onset and a highly elevated serum creatinine kinase level is highly suggestive for cancer-associated myositis, given the presence of an untreated pancreas carcinoma. Toxic- or drug induced myopathies were not fully excluded because the patient was treated with statins. However there was further worsening of the myositis despite stopping the statine therapy and only high dose glucocorticoids could lower the creatinine kinase level. The rhabdomyolysis could also be contrast-induced after ERCP (8), although renal function always remained normal. Nevertheless, it is remarkable that the patient presented with the myositis only a couple of days after the endoscopic ultrasound and the ERCP, which may suggest that seeding of tumour cells during the procedure has triggered the onset of the myositis. In patients with pancreatic adenocarcinoma, Levy et al. (9) measered a significant increase in plasma concentrations of cell-free DNA (cfDNA) and detection of KRAS mutations after EUS-FNA as markers of tumoremia. It would be interesting to evaluate if these markers are associated with an increase of the creatinine kinase levels or specific anti-tumoural autoantibodies in patients with paraneoplastic syndromes. Unfortunately, we could not obtain a previous measurement of the creatinine kinase level in our case. Because of its total regression after surgical resection of the tumour, we

do consider this case an example of a paraneoplastic syndrome. An indicative muscle biopsy could have confirmed our diagnosis.

Because the number of cases is limited, the pathogenesis of pancreatic cancer associated myositis remains unclear and medical treatment is mostly based on the therapy of inflammatory myopathies with glucocorticoids as first choice. Presumably, the immune process is driven by anti-tumoural autoantibodies with cross reactivity to muscle antigens. A cohort study in patients with idiopathic inflammatory myopathies showed that some myositis-specific antibodies (e.g. anti-TIF1-γ, anti-NXP2 and anti-SAE1 antibodies) are associated with an increased risk of cancer (10). The pathophysiological link between these specific autoantibodies and the tumour still needs to be clarified.

Despite complete regression of the myositis, both the histology as well as the presentation with a paraneoplastic myositis is associated with an unfavourable prognosis. A retrospective study by Pellat et al. suggests a positive effect of adjuvant chemotherapy combining etoposide and platinum derivatives in resected digestives NECs (11), but further studies are needed to confirm this. This case illustrates that neuroendocrine tumours present themselves with marked clinical and biological heterogenity. Therefore, scientific guidance in defining the treatment strategy is often inadequate, which can lead to significant differences in treatment preferences between experts and centers (12).

In conclusion, a case of paraneoplastic myositis associated with pancreatic neuroendocrine carcinoma is reported here. The development of muscle weakness in a patient with pancreatic cancer should raise suspicion for this rare phenomemon. Besides glucocorticoids, resection of the tumour can lead to complete regression of the myositis. Treatment delay should be avoided because of the great impact of immobility on the quality of life of the patient and on the operability. Furthermore, both the tumour type as well as the presence of a paraneoplastic syndrome predict an unfavourable prognosis, which may warrant adjuvant chemotherapy.

Acknowledgments

We thank Isabelle Maurissen, M.D. for her comments on the editing of this article.

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