# Sarcoidosis-like disease with pulmonary infestation, meningoencephalitis and transverse myelitis after sigmoid cancer treatment

C. Callens[1,2], H. De Cauwer[1,2], M. Viaene[2], D. Vanneste[3], A. Eyben[4], D. Coeman[5]

(1) Faculty of Medicine and Health Sciences. University of Antwerp, Wilrijk, Belgium; (2) Dpt. of neurology, AZ St Dimpna, Geel, Belgium; (3) Dpt. of radiology, AZ St Dimpna, Geel, Belgium; (4) Dpt. of gastroenterology, AZ St Dimpna, Geel, Belgium; (5) Dpt. of pneumology, AZ St Dimpna, Geel, Belgium.

## Abstract

**We present the case of a 40-year-old male with recent history of moderately differentiated invasive adenocarcinoma of the sigmoid in whom both respiratory and neurological disease developed simultaneously, mimicking diffuse metastatic disease. The broad differential diagnosis and pitfalls (both diagnostic and therapeutic) are described. Pulmonary sarcoidosis as well as neurosarcoidosis occur very rarely after solid cancers.** (Acta gastroenterol. belg., **2021,** 84**, 672-674**).

**Key-words**: neurosarcoidosis, meningoencephalitis, transverse myelitis, differential diagnosis, sigmoid cancer, chemotherapy.

## Introduction

We report on an intriguing case of a male patient with recent history of moderately differentiated invasive adenocarcinoma of the sigmoid in whom both respiratory and neurological disease developed simultaneously.

We describe the differential and final – very uncommon – diagnosis and the pitfalls.

## Case history

A 40-year-old male was admitted to the neurology ward because of rapidly ascending sensory disturbances and paraparesis with urinary retention since ten days, accompanied by headache, fever, nausea, vomiting and photophobia since four days. Seven months earlier, he was diagnosed with moderately differentiated invasive adenocarcinoma of the sigmoid.

This tumor was staged pT3N0M0, but was associated with Isolated Tumor Deposits (ITD) in the pericolic adipose tissue and microscopic venous invasion, thus categorized as a high- risk stage II colorectal tumor (1).

As a result, the Multidisciplinary Tumor Board (MTB) advised adjuvant FOLFOX chemotherapy

CT thorax was normal: there were no signs of pulmonary metastatic disease.

The adenocarcinoma was curatively treated by laparoscopic resection followed by adjuvant FOLFOX chemotherapy which was stopped after one cycle because of 5-FU-induced cardiomyopathy. Oncological follow-up with CT scan of chest and abdomen two weeks prior to admission had shown a few small mediastinal, hilar and intrapulmonary lymph nodes without signs of locoregional recurrence of the sigmoid carcinoma.

Clinical examination showed meningeal irritation, hyperreflexia and flaccid paraparesis with Th12 sensory level. MRI of the brain and spinal cord showed multifocal leptomeningeal enhancement with diffuse confluent T2-hyperintense medullary lesions and inflammation of the paraspinal muscles (Figure 1, 2). Lumbar puncture showed lymphocytic pleocytosis (703/µL) with hypoglycorrhachia and elevated protein level (225 mg/dL).

Diagnosis of meningoencephalitis with transverse myelitis was established and empirical treatment with high-dose intravenous corticosteroids (1 gram of IV methylprednisolone 1dd for 5 days) and quadruple antimicrobial therapy (amoxicillin, ceftriaxone, ciprofloxacin, acyclovir) was initiated. Histopathological examination of the CSF showed atypical cells without the possibility for further immunohistochemical differentiation. Because meningitis carcinomatosa was suspected, treatment with FOLFIRI chemotherapy and panitumumab was started. Repeat lumbar punctures failed to confirm the presence of atypical cells. Extensive PCR testing and serological work-up of blood and CSF did not reveal any causative infectious agent nor autoantibody. Gram stain and cultures for aerobic and anaerobic bacteria remained negative. Intracellular and extracellular antineuronal autoantigens (NMDAR, CASPR2, LGI1, GABAbR, AMPAR) were all negative. Antimicrobial therapy was stopped and corticosteroids were tapered.

Almost simultaneously with neurological deterioriation, imaging of the lungs showed increasing lung pathology: with hilar and mediastinal lymphadenopathy, the presence of multiple intrapulmonary nodules, pleural effusion and alveolar consolidation: differential diagnosis of diffuse infective or inflammatory or metastatic disease. The alveolar consolidation faded after initiating meropenem.

Imaging of the abdomen did not reveal evidence for neither tumor recurrence nor metastatic disease.

Unfortunately, after initial stabilization his condition further worsened to tetraparesis with C3 sensory level, bilateral blindness and severe neuropathic pain in both legs. MRI of the brain and spinal cord showed

Correspondence to: H. De Cauwer, Dpt. of neurology, AZ St Dimpna, JB Stessenstraat 2, 2440 Geel, Belgium. Faculty of Medicine and Health Sciences. University of Antwerp, Wilrijk, Belgium. Phone: +32(0)14.57.70.18.
E-mail: harald.decauwer@ziekenhuisgeel.be

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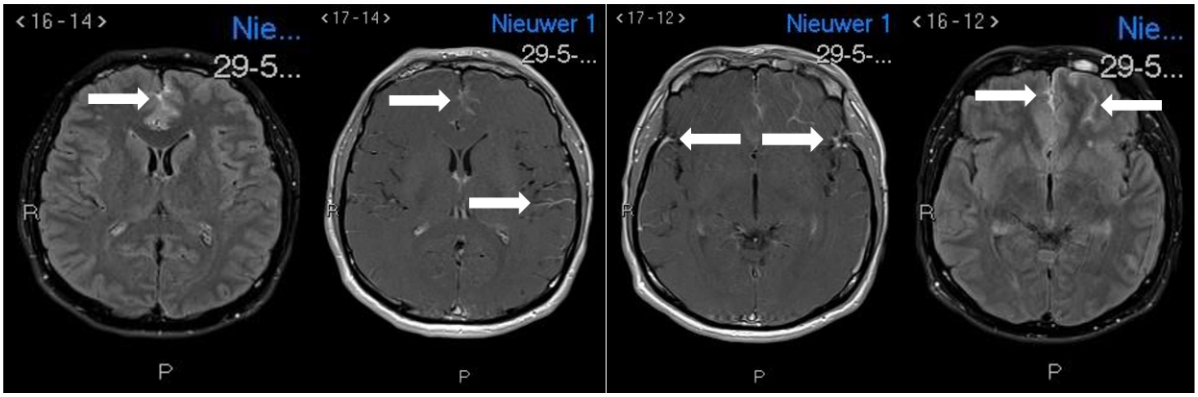


Figure 1. — Axial T1- and T2-weighted-Fluid-Attenuated Inversion Recovery show multifocal leptomeningeal enhancement mostly at the left frontal lobe and centrally in the cerebellum.

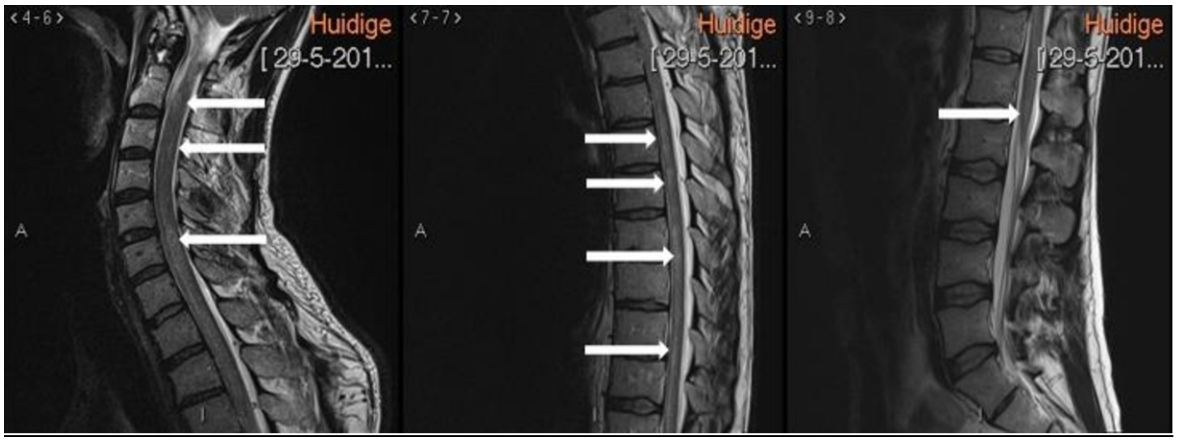


Figure 2. — Sagittal T2 weighted images showing multifocal leptomeningeal enhancement with diffuse confluent T2-hyperintense medullary lesions on several levels, myelitis with extensive edema, less pronounced at the control exam with disappearance of the myelum edema (cervical (left), thoracic (middle) and lumbar (right) level).

multiple new multifocal T2-hyperintense cerebral and medullary lesions with resolution of the leptomeningeal enhancement and paraspinal muscle inflammation. Because of underlying auto-immune reaction (e.g. acute demyelinating encephalomyelitis (ADEM)) was suspected high-dose corticosteroids were restarted, because of lack of clinical effect followed by a five-day course of intravenous immunoglobulins (IVIg) (0.4 gram per kilogram) which started on day 20 after admission. With this treatment, rapid clinical improvement was seen with complete resolution of blindness, marked recovery of upper limb strength and Th8 sensory level.

Whole body FDG-PET/CT on day 30 after admission showed a consolidation in the right lower lobe of the lung with retro-obstructive atelectasis and multiple FDG-avid nodular lesions in both lungs. Control MRI 5 months after admission showed clear improvement (figure 1,2).

Bronchoscopy with aspiration and biopsy of right lower lobe ostium came back negative for malignancy. He was discharged to the rehabilitation center after two months in a stable condition with flaccid paraparesis and associated sensory disturbances, neuropathic pain and urinary retention. Transbronchial biopsy of mediastinal lymph nodes revealed noncaseating granulomata, suggestive for sarcoidosis.

Because of both neurological and pneumological stable situation after IvIg, no further therapy was started. He is still following multidisciplinary rehabilitation therapy. After oneyear he is still suffering from paraparesis and atonic bladder. The neuropathic pain has ameliorated.

## Discussion

This case is intriguing as a couple of months after the first regimen of chemotherapy in this patient was terminated because of suspected cardiotoxic effect (with complete remission afterwards), both respiratory and neurological disease developed simultaneously.

A neurotoxic effect of chemotherapy was unlikely. Atonic bladder and Lhermitte sign (an intense burst of pain like an electric shock that runs down your back into the 4 limbs when a person moves the neck) as a consequence of cervical dorsal column dysfunction were reported earlier in patients treated for colorectal carcinoma. However, these appeared during the chemotherapy, did not show

cerebral or spinal MRI alterations, and resolved a few weeks after the discontinuation of oxaliplatin (2).

Differential diagnosis included metastatic disease and a paraneoplastic phenomenon. Both were unlikely because of the clinical course respectively the absence of specific anti-neuronal antibodies.

Moreover, as initially meningitis carcinomatosis was suspected to be the underlying cause of the paraparesis and painful peripheral neuropathy, a second regimen of chemotherapy was started. Unfortunately, rapid and impressive neurological (blindness, quadriplegia) and pneumological deterioration was noticed.

Infections known to cause spastic paraparesis as well as pulmonary sarcoidosis-like syndrome, were excluded. Hepatitis A serology was weakly positive and has been described in transverse myelitis, but was negative on repeat serological testing. Other pathologies like posterior reversible encephalopathy syndrome (PRES) and leukoencephalopathy related to 5-fluorouracil and oxaliplatin-use, were not likely in our case (3-5).

Distant malignancies may cause granulomatous pulmonary lymphadenitis, yet oncological investigations remained negative at different control exams.

The favourable effect of IVIg on cerebral and spinal alterations was striking. Sarcoidosis mimics ADEM and Devic's (neuromyelitis optica) disease especially in transverse myelitis cases, however in our case CSF pleocytosis and hypoglycorrhachia, pulmonary involvement with multiple adenopathies showing granulomatous inflammation, and the absence of aquaporin-4-immunoglobulin G, all suggested sarcoidosis.

Because of both neurological and pneumological stable situation after IvIg, no further therapy was started.

The involvement of both lungs, nervous system and paraspinal muscles (most probably sarcoid myopathy) supports the diagnosis of sarcoidosis, which is only sporadically linked to chemotherapy thusfar (6,7).

The debate is still ongoing in literature. Grados et al. suggest that sarcoidosis is merely an immune reaction after cancer / cancer therapy and that sarcoidosis, although extremely rare, must be considered in the differential diagnosis of patients with a history of malignancy who have developed lymphadenopathy or other lesions (8). Histological confirmation of cancer relapse is mandatory in order to avoid unjustified treatments.

However, patiënts included in their retrospective case study were in remission after breast, lung, colorectal, or head and neck cancers and 33.3% of these patients did not receive any chemotherapy. Those who were exposed to chemotherapy received many different drugs, so the development of sarcoidosis in these patients could not be explained by chemotherapy alone.

Therefore, Grados et al. suggest this association should even be considered as a protective factor against cancer relapse (8).

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**Conflict of interest**

All the authors report no disclosure nor conflict of interest relevant to the manuscript. All authors report no financial disclosure.

**Ethical approval**

This manuscript does not contain any studies with human participants or animals performed by any of the authors.

**Informed consent**

Informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this article.

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