Reminder of important clinical lesson

Enteropathy associated T-cell lymphoma resulting in restrictive cardiomyopathy and mimicking myocardial infarction

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Summary

A 64-year-old woman was referred with a short history of abdominal pain, anorexia and weight loss. Investigations revealed a probable enteropathy associated T-cell lymphoma (EATL). Further investigations revealed evidence of what appeared to be a myocardial infarction. After going through laparoscopy to obtain diagnostic tissue, the patient developed cardiogenic shock which proved refractory to medical therapy. Postmortem examination revealed diffuse abdominal lymphoma consistent with EATL. Surprisingly, there was extensive infiltration of the myocardium. This report demonstrates an unusual pathology resulting from EATL and discusses the limited evidence relating to cardiac involvement of this disease.

BACKGROUND

This case highlights the rapid and unpredictable progression of a rarely encountered disease entity: enteropathy associated T-cell lymphoma (EATL). While the diagnosis of EATL was suspected at presentation, tissue conformation remained elusive, and, because of this, a rare complication of the disease was not identified. Although it is unlikely that further progress in diagnosis and staging would have altered the natural history of this patient's disease, it highlighted to us the importance of accepting and incorporating new data while managing the immediate clinical issues.

CASE PRESENTATION

A 64-year-old woman was referred to with a 6-week history of anorexia and weight loss. Gastroscopy revealed scalloped duodenal mucosa consistent with coeliac disease, and histology confirmed the presence of an enteropathy. On basis of the results of initial blood tests, it was decided to admit the patient for investigation of a probable EATL.

Her symptoms had been progressive for 4 months; anorexia had been followed by cramping abdominal pain, persistent vomiting and significant weight loss. She took no regular medication. She had a 25-pack-year history of smoking and only occasionally drank alcohol. Her family history was relevant only for a sister who had died at the age of 65 as a result of gastric cancer.

Examination revealed a pale, emaciated lady. Her body mass index was 16.3 kg/m². She was tachycardic at 108 beats per minute (bpm), and her blood pressure was 90/48 mm Hg. Mild left-hypochondrial tenderness was the only clinical finding. Her haemoglobin was 8.9 g/dl, white cell count 13.4×10⁹/l, neutrophils 10.5×10⁹/l and platelets 670×10⁹/l. Her renal function was normal, total protein was 71 g/l, albumin 23 g/l, lactate dehydrogenase 697 IU/l, Alk

phos 138 IU/l and aspartate aminotransferase 42 IU/l. Her erythrocyte sedimentation rate was 120 mm/h. Her IgA antiendomysial antibodies and tissue transglutaminase were negative.

INVESTIGATIONS

A routine ECG surprisingly demonstrated ST segment elevation in leads II, III, aVF and V4-V6, findings that were most consistent with an acute inferolateral myocardial infarction (figure 1). However, she was asymptomatic and denied ever having symptoms of angina. Her troponin T was elevated at 0.66 ng/ml. Echocardiography demonstrated moderate left-ventricular function, left-ventricular hypertrophy and hypokinesis of the lateral wall of the left ventricle. Coronary angiography demonstrated a chronic total occlusion of the right coronary artery and moderate atheromatous disease in the left anterior descending artery. There were no acute lesions seen. She received a red-cell transfusion to alleviate any anaemia-induced cardiac ischaemia.

Abdominal ultrasonography revealed no obvious visceral pathology, but an abdominal CT revealed an abnormal loop of small bowel within the left flank, with mural thickening and stranding of the surrounding fat. There were adjacent subcentimetre lymph nodes but no gross disease in the abdomen or thorax. The findings were felt to be consistent with a lymphoma of the small bowel. Note was made of thickened left-ventricular muscle with irregular attenuation on CT. Enteroscopy was attempted but could not progress beyond the proximal jejunum, and no tissue was obtained for diagnostic purposes. As a result, she underwent a diagnostic laparoscopy which demonstrated a large inflammatory mass with adhesions to the abdominal wall. It was not felt to be safely possible to

Figure 1 Patient's admission ECG.

Figure 2 Gross myocardial specimen demonstrating tumour deposits within the myocardium (black arrows).

obtain tissue for diagnostic purposes during the procedure and laparotomy was advised.

OUTCOME AND FOLLOW-UP

Postoperatively, she was tachycardic at 110 bpm, hypotensive at 65/46 mm Hg, oliguric and anaemic at 7.3 g/dl. Intravenous fluid resuscitation failed to correct the physiological deficits and the patient's condition deteriorated. She was transferred to the intensive care unit, transfused red cells and commenced on antibiotics and inotropes. She developed pulmonary oedema, for which she was given frusemide, and rapid atrial fibrillation which settled with intravenous amiodarone. Her troponin was elevated at 1.6 ng/ml, but there was no progression of the ECG changes which had been identified on admission. Echocardiography

now revealed an ejection fraction of less than 20% with anterior and posterior-wall hypokinesia. A presumptive diagnosis of coronary reinfarction with cardiogenic shock was made. Her shock proved refractory to intensive medical therapy, and she died in the intensive care unit.

Postmortem examination revealed a fungating, necrotic lymphoma of the small intestine involving the adjacent mesentery. There were deposits in both kidneys and within the wall of the left ventricle (figures 2 and 3). In multiple areas the tumour demonstrated angiotrophic tendencies but was never seen to invade the intravascular space. Immunohistochemistry of the tumour revealed CD3 and CD8 positivity; CD4 was weakly positive, and CD20 and CD56 were negative. T-cell receptor gene rearrangement studies demonstrated a TCR β and γ clonal-cell population, findings

Figure 3 Low-power microscopic view of the heart demonstrating thrombus (Black arrow) within an atherosclerotic coronary artery (white arrow), normal myocardium (black arrowhead) and T-cell lymphoma (white arrowhead).

characteristic of EATL. The heart showed moderate coronary artery disease and an area of fibrosis consistent with an old infarct. There was no evidence of a recent infarct; however, the myocardium was extensively infiltrated by lymphoma.

DISCUSSION

Enteropathy associated T-cell lymphoma is one of the most problematic diseases encountered by gastroenterologists. Despite being the most common intestinal T-cell lymphoma, it is rare, with an estimated incidence of 0.1 per 100 000 in Western populations.^{1–3} It can be easily missed, as only half of EATL cases have a previous diagnosis of coeliac disease. Even among those who have a diagnosis of coeliac disease, the histology is variable and can overlap with refractory coeliac disease or ulcerative jejunitis.^{4–5} Finally, even with a diagnosis, the treatment options are limited; EATL responds poorly to chemotherapy or stem-cell transplantation, and the most recent literature estimates the 2-year survival at less than 20%.^{6–8}

In our patient's case, despite rapid recognition of the disease, appropriate investigation and numerous attempts to obtain diagnostic tissue samples, we failed to confirm the diagnosis prior to her death. What was unusual about our patient's case was the presence of cardiac involvement that escaped diagnosis and that contributed to her death.

The literature relating to EATL suggests that 20% of patients will present with Ann Arbor stage IV disease, commonly involving the lungs, liver, spleen or bone marrow.^{6–9} However, large autopsy series of patients with non-Hodgkin's lymphoma have identified cardiac involvement in approximately 20% of cases.^{10–11} Even among solid organ

tumours, myocardial metastases are present in up to one quarter of cases at postmortem, most commonly arising from melanoma, breast or lung. However, these cardiac metastases are usually asymptomatic and are rarely a terminal event, and as a result, they are rarely sought or diagnosed.¹² Curiously, the published literature relating to EATL has not frequently documented this complication, which may suggest that EATL has a lower rate of cardiac involvement than other forms of NHL. Indeed, cardiac disease arising from EATL has only been documented in one patient among a single case series.⁶

Our patient's case became more unusual when ECG changes suggested an acute myocardial infarction and echocardiography demonstrated findings consistent with ischaemic heart disease. Confounding the diagnosis of lymphomatous cardiac involvement was the concurrent presence of atheromatous disease in the coronary vasculature on angiography, a finding that the postmortem confirmed in addition to demonstrating mural fibrosis consistent with previous myocardial infarction. Cardiac involvement by tumour frequently results in ECG changes, but it is rare to see ST segment alterations mimicking a myocardial infarction.^{12–13} Furthermore, echocardiography, which is reported to be the radiological modality of choice for the investigation of cardiac metastases, especially in the left-ventricular wall, failed to demonstrate the lesions in this instance.¹⁴

We should perhaps have been suspicious of the diagnosis of coronary artery disease in a patient who was asymptomatic from a cardiac point of view, whose ECG changes failed to progress with time and who was under investigation for an EATL. However, the concurrent diagnosis of coronary

artery disease, made with electrocardiographic, biochemical, angiographic and echocardiographic evidence masked this rare complication of a rare disease.

Learning points

- ▶ EATL is a rare disease that can easily be overlooked.
- ▶ Cardiac involvement is thought to occur in up to 20% of lymphoma cases but is rarely symptomatic and infrequently associated with terminal events.
- ▶ Data must be interpreted in the appropriate clinical context. Attributing abnormal investigation results to a previously known disease must be done with caution in the setting of a new unrelated presentation.

Competing interests None.

Patient consent Obtained.

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