Somato Publications ISSN: 2643-2609

Annals of Gastroenterology and Digestive Disorders

Case Report

Non-Portal Hypertension Ascites - Azathioprine Induced Non-Hodgkin Lymphoma in a Heart Transplant Patient

Georgia Haughton* and Mohammed Fareeth

Acute and Internal Medicine, Acute medical unit, Royal Blackburn Hospital, UK

*Address for Correspondence: Georgia Haughton, Acute and Internal Medicine, Acute medical unit, Royal Blackburn Hospital, UK, E-mail: georgiahaughton@gmail.com

Received: 05 January 2023; Accepted 24 January 2023; Published: 28 January 2023

Citation of this article: Haughton, G., Fareeth, M. (2023) Non-Portal Hypertension Ascites - Azathioprine Induced Non-Hodgkin Lymphoma in a Heart Transplant Patient. Ann Gastroenterol Dig Dis, 6(1): 01-05.

Summary

Lymphomas are a group of malignancies that arise from lymphocytes the blood, typically presenting with non-tender lymphadenopathy and B-symptoms. It is commonly recognised that immunosuppressive drugs increase the risk of developing lymphoma.

Here, we present a 70-year-old male admitted with abdominal ascites, vomiting and acute kidney injury. He had a background of cardiac transplantation 21 years ago. Of note he was taking long term azathioprine. Ascitic fluid analysis and CT thorax, abdomen and pelvis showed findings consistent with non-Hodgkin lymphoma. In this case the patient presented in an atypical manner with no peripheral lymphadenopathy or B-symptoms. It is rare for lymphoma to present with ascites.

This case emphasises the importance of paracentesis, a relatively safe and cost-effective procedure. In this case, cytology was able to support radiological diagnosis of lymphoma. Multiple studies have shown a link between renal transplant immunosuppressive therapies and developing lymphoma. However, there is very little information around this topic in cardiac transplants.

Background

Lymphoma is an umbrella term for a group of malignancies that arise from lymphocytes in the blood. The most common type is non-Hodgkin lymphoma, which can again be divided into further subtypes. Non-Hodgkin lymphoma is the 6th most common malignancy in the UK [1], most commonly affecting the elderly. Risk factors for developing lymphoma include infection such as EBV and hepatitis B and C, alongside chronic immunosuppression [2]. Lymphoma typically presents with non-tender lymphadenopathy and B-symptoms including night sweats, fevers, fatigue and weight loss.

It is commonly recognised that the use of immunosuppressive drugs increases the risk of developing lymphoma, in particular non-Hodgkin's lymphoma [3]. Multiple studies have identified a correlation between the use of azathioprine in both autoimmune disease and for immunosuppression in patients who have had organ transplants and the development of lymphoma [3,4].

In this case, we present a patient who took azathioprine for immunosuppression following his cardiac transplant. He subsequently developed lymphoma that presented in a non-typical fashion.

Case Presentation

A 70-year-old male presented with a one-day history of intermittent nausea and vomiting. He also had reduced oral intake and lack of appetite. He reported no abdominal pain, changes in bowel habits or haematemesis.

The patient had a significant medical background consisting of ischaemic heart disease (requiring cardiac transplantation in 2001), hypertension, chronic kidney disease stage 3, gastroesophageal reflux, hypothyroidism, diverticular disease and colonic polyps. His regular medications were folic acid 5mg, pravastatin 20mg, levothyroxine 75mcg, ezetimibe 10mg, temazepam 10mg, lansoprazole 30mg and senna 7.5mg. Of note, he also took azathioprine 75mg in the morning and 50mg at night.

The man lived alone and had carers once a day. He was relatively dependent on others and was only able to leave the house with his mobility scooter due to his limited mobility. He was an ex-smoker of 20 pack years and did not drink alcohol.

On examination his observations were all within normal ranges, apart from a mild tachycardia of 103 BPM. Physical examination was unremarkable revealing only a slightly distended abdomen that was soft and not tender. There was no peripheral lymphadenopathy.

Investigations

His chest x-ray was unremarkable except for findings consistent with a previous sternotomy (Table 1). Ultrasound abdomen revealed right sided hydronephrosis and ascites. An ascitic tap was then performed revealing the below results (Table 2 and Figure 1). Ascitic fluid results made it unlikely that portal hypertension was the cause of this man's ascites. The results were suggestive of malignancy, in particular lymphoma. The CT findings also supported a diagnosis of lymphoma. Additionally, the patient was found to have bilateral pleural effusions and a right sided pulmonary embolism.

The patient had ongoing anaemia during his admission; this would

Table 1: Blood results from the patient at day 1 and day 14 of admission.

Blood results	Normal range	On admission	Day 14 of admission
Hb (g/L)	130-180	102	92
WCC (x10 9 /L)	4-11	5.2	9.7
CRP (mg/L)	<5	203	161
Neut (x10 9/L)	2-7.5	4.2	8.4
Na+ (mmol/L)	133-146	137	163
K+ (mmol/L)	3.5-5.3	5.6	4.9
Ur (mmol/L)	2.5-7.8	36.4	34.3
Cr (umol/L)	68-150	420	267
eGFR	>90	11	22
Bilirubin (um/L)	3-17	17	48
Albumin (g/L)	33-49	34	22
ALT (u/L)	10-50	10	17
LDH (u/L)	10-250	2900	

have ideally been investigated with bone marrow analysis. Unfortunately, the patient was haemodynamically unstable throughout his admission which made performing the procedure difficult and high risk. This was discussed with the haematology team who advised that in this case the clinical diagnosis was clear and bone marrow analysis would add little to what was already known.

The haematology team did advise performing a lymph node biopsy. However, it was decided that this would not add any further clinical knowledge given the fact that the ascitic fluid cytology had already been sent and there was radiological evidence suggesting malignancy. Although FACS would have been useful to diagnose the disease from a histological perspective, it was unfortunately not feasible in this case.

Treatment

Originally, the patient was treated for an acute kidney injury with intravenous fluids (0.9% sodium chloride) and holding of nephrotoxic drugs. He was also diagnosed with sepsis of unknown origin due to his high CRP and tachycardia - this was treated with IV Tazocin and blood results improved.

The CT scan revealed a multitude of other problems, all of which were likely due to his underlying lymphoma. The patient was treated with low molecular weight heparin for his pulmonary embolism. Both his ascites and pleural effusions were managed with drains and albumin infusions for symptomatic relief. The albumin infusions were thought to be the cause of the patients hypernatraemia. Bilateral nephrostomies were inserted when an obstructive cause of acute kidney injury was identified.

Unfortunately, despite best attempts, and administration of corticosteroids, the patient continued to deteriorate and his clinical condition worsened. He was reviewed by intensive care who explained that given his poor baseline he would not be suitable for level 2 or 3 care, and it was decided that a DNAR form would be put into place. Haematology also assessed the patient and explained that given his current frailty and multi-organ failure he would not be a candidate for chemotherapy to treat his non-Hodgkin lymphoma.

Table 2: Ascitic fluid analysis in keeping with malignancy, most likely lymphoma.

Protein	34g/L
Albumin	18g/L
SAAG	<1.1mmol/L
LDH	9574
Neutrophil	600/uL
Cytology	Large number of CD45-positive lymphoid cells

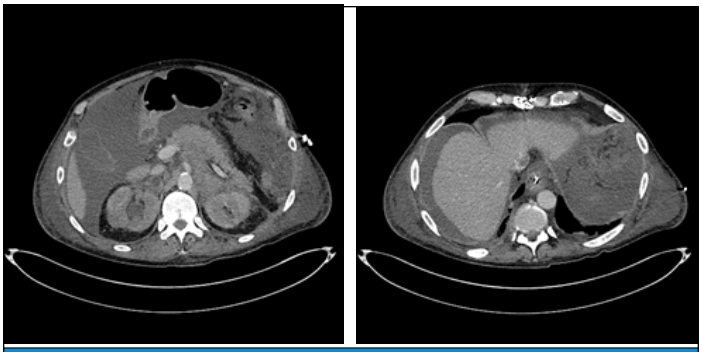

Figure 1: CT scan of the thorax, abdomen and pelvis showing extensive retroperitoneal soft tissue which encased the renal collecting system causing obstruction. Extensive omental and mesenteric infiltration with a large volume of free fluid.

The patient was managed with best supportive, and eventually palliative care.

Outcome and Follow-up

17 days into his admission the patient passed away.

Discussion

The patient in this case did not present typically for non-Hodgkin lymphoma. There was no peripheral lymphadenopathy and the patient denied any B-symptoms. Examination and investigation revealed ascites - it is rare for lymphoma to present with ascites and throughout my research I have found only a small number of reports of abdominal ascites being the primary clinical presentation [5-8]. The patient's initial presentation of vomiting and renal obstruction was likely due to the mass effect of the lymphoma in his abdomen.

Studies have shown a clear link between immunosuppressive therapies in transplant patients and the development of non-Hodgkins lymphoma [3], with one study estimating that around 2% of renal transplant patients will develop the disease [9]. Long term use of azathioprine for immunosuppression in multiple conditions, including solid organ transplants and rheumatoid disease, has been linked to the development of lymphoma [3,4,10].

The patient in this case had been taking azathioprine for many years following his heart transplant surgery. There is, however, little information around this topic in cardiac transplants, and our case appears to be one of the first reported. The studies that we did find supported our own findings [11,12]. Some studies have even hypothesised that transplant patients who have had heart transplants are at the highest risk of developing lymphoma [13,14]. This is an area that will hopefully become more recognised in the coming years.

It is important to acknowledge a couple of points in this case. Firstly, it is not possible to be certain that azathioprine was the definitive cause of lymphoma in this patient; it is important to keep an open mind when considering causative factors. However, there did not appear to be any other clear risk factors for the development of lymphoma in this gentleman. It is also important to remember that although clinical and radiological evidence, alongside paracentesis were all highly indicative of lymphoma, there was no tissue biopsy to confirm this diagnosis.

This case emphasises the importance of performing paracentesis when patients present with free fluid in the abdomen. Not only does this guide clinicians in determining whether the cause of the ascites is hepatic in nature or not, but also allows them to consider important differentials such as malignancy and infection. Ascitic taps are not only relatively safe and simple procedures, but are also cost effective and provide clinicians with a great deal of information. In this case, cytology of the fluid was able to support radiological diagnosis of lymphoma.

Learning Points

1. This case adds to the ever-increasing evidence of an association between immunosuppressive drugs and the development of lymphoma in transplant patients.
2. Ascites is a rare but reported presentation of lymphoma. Thus, there should be a low clinical suspicion for suspecting lymphoma in immunosuppressed patients who present with non-specific abdominal distention.
3. Paracentesis is a simple and cost-effective test that provides important clinical information when assessing a patient with ascites.

References

1. https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/nonhodgkinlymphoma#:~:text=Non%2DHodgkin%20Lymphoma%20(NHL)%20incidence&text=Non%2DHodgkin%20lymphoma%20is%20the,-year%20(2016%2D2018).
2. Zhang, Y., Dai, Y., Zheng, T., Ma, S. (2011) Risk factors of non-Hodgkin's lymphoma. Expert Opinion on Medical Diagnostics, 5(6): 539-550.
3. Na, R., Laaksonen, MA., Grulich, AE., Meagher, NS., McCaughan, GW., Keogh, AM., et al. (2016) Iatrogenic immunosuppression and risk of non-Hodgkin lymphoma in solid organ transplantation: A population-based cohort study in Australia. Br J Haematol, 174(4): 550-562.
4. Pitt, P., Sultan, A., Malone, M., Andrews, V., Hamilton, E. (1987) Association between Azathioprine Therapy and Lymphoma in Rheumatoid Disease. J R Soc Med, 80(7): 428- 429.
5. Vakar-Lopez, F., Yang, M. (1992) Peripheral T-cell lymphoma presenting as ascites: A case report and review of the literature. Diagn Cytopathol, 20(6): 382-384.
6. Liu, E., Wang, J., Yang, W. (2019) Peritoneal lymphoma with ascites mimicking portal hypertensive ascites. Medicine, 98(8): e14583.
7. Das, D. (2006) Serous effusions in malignant lymphomas: A review. Diagn Cytopathol, 34(5): 335-347.

8. Al-Nabulsi, M., Basnet, A., Salerno, V., Cholankeril, M. (2016) A case of mantle cell lymphoma presenting with ascites. Clin Case Rep, 4(4): 399-403.

9. Bates, W., Gray, DW., Dada, MA., Chetty, R., Gatter, KC., Davies, DR., et al. (2003) Lymphoproliferative disorders in Oxford renal transplant recipients. J Clin Pathol, 56(6): 439-446.

10. Patel, P., Moazzam, N., Potti, A., Mehdi, SA. (2005) Azathioprine induced Hodgkin lymphoma: A case report and review of literature. Am J Clin Oncol, 28(4): 427-428.

11. McMullan, DM., Radovaneevic, B., Jackow, CM., Frazier, OH., Duvic, M. (2001) Cutaneous T-cell lymphoma in a cardiac transplant recipient. Tex Heart Inst J, 28(3): 203-207.

12. Nassif, S., Ozdemirli, M. (2013) EBV-positive low-grade marginal zone lymphoma in the breast with massive amyloid deposition arising in a heart transplant patient: A report of an unusual case. Pediatr Transplant, 17(6): 141-145.

13. Domingo-Domenech, E., De Sanjose, S., Gonzalez-Barca, E., Romagosa, V., Domingo-Claros, A., Gil-Vernet, S., et al. (2001) Post- transplant lymphomas: A 20-year epidemiologic, clinical and pathologic study in a single center. Haematologica, 86(7): 715-721.

14. Opelz, G., Dohler, B. (2004) Lymphomas after Solid Organ Transplantation: A Collaborative Transplant Study Report. Am J Transplant, 2004; 4(2): 222-230.