

# Unexpected Systemic Amyloidosis in Patient With Restrictive Cardiomyopathy

Gabrijela Stanić<sup>1</sup>, Dubravka Jandrić<sup>1</sup>, Rosana Troskot Perić<sup>2,3,4</sup>, Marinko Marušić<sup>2,3,4</sup>, Mia Knobloch<sup>2</sup>

<sup>1</sup> Department of Pathology and Cytology, Clinical Hospital »Sveti Duh« Zagreb, Zagreb  
gabrijela\_stanic@yahoo.com

<sup>2</sup> Department of Gastroenterology and Hepatology, Clinical Hospital »Sveti Duh« Zagreb

<sup>3</sup> Faculty of Medicine, Josip Juraj Strossmayer University of Osijek, Osijek

<sup>4</sup> Faculty of Health Studies, University of Rijeka, Rijeka

## ABSTRACT

*Systemic amyloidosis is a rare disease and it is caused by deposition of insoluble abnormal fibrillary proteins known as amyloid in extracellular space. Protein deposits are components of immunoglobulins produced by plasma cells and B-lymphocytes in response to antigenic stimulation. Three different forms of amyloidosis can be distinguished, the primary (AL), secondary (AA) and family form. Localized amyloidosis occurs in the pancreas in type 2 diabetic patients and in patients on chronic hemodialysis. The clinical presentation in amyloidosis depends on the affected organs. Symptoms are non-specific and included fatigue, weight loss, nephrotic syndrome, restrictive cardiomyopathy with thickening of the interventricular septum and ventricular wall, peripheral neuropathy, hepatomegaly, macroglossia, purpura and bleeding diathesis. In these article we presented the unexpected systemic amyloidosis in a patient with restrictive cardiomyopathy and without malignant and hematological diseases who suffered from dyspnea, weakness, fatigue loss of appetite and cough. Diagnosis of systemic amyloidosis was made upon histological samples after autopsy.*

**Key words:** amyloid, systemic amyloidosis, gastrointestinal tract, cardiomyopathy, kidney failure

## Introduction

Systemic amyloidosis is a rare disease and it is caused by deposition of insoluble abnormal fibrillary proteins known as amyloid in extracellular space<sup>1</sup>. Three different forms of amyloidosis can be distinguished, the primary (AL), secondary (AA) and family form. Localized amyloidosis occurs in the pancreas in type 2 diabetic patients and in patients on chronic hemodialysis<sup>1-4</sup>.

This is a disease of older adults and the median age at diagnosis is about 60 years.

The clinical presentation in amyloidosis depends on the affected organs and the symptoms are usually nonspecific.

## Case presentation

A 64 years old female presented to the University Hospital with two month history of progressive dyspnea, weakness, fatigue loss of appetite and cough. The patient had a past medical history of heart failure with pericardial and pleural effusion two months prior to presentation.

The patient developed weakness, progressive dyspnea and a cough. The cardiological outpatient diagnosis and treatment indicated a progressive heart failure. MSCT and MR showed ascites and calcified lymph nodes in abdomen.

Myelogram was normal. Complete gastroenterology exam showed no signs of malignancy. Clinical condition of the patient was bad and despite all measures, parenteral diet and supporting therapy patient died of cardiac failure and malnutrition.

Autopsy showed ascites, pleural and pericardial effusion, pulmonary edema, dilated and increased heart, pancreas with fibrosis and calcification of the surrounding fatty tissue. Abdominal lymph nodes were enlarged and calcified. The small and large intestine were edematous. Histological examination showed amyloid deposits and thickening of the wall of the blood vessels in the myocard, thyroid gland, liver (Figure 1, 2 and 3), kidneys and lungs. Amyloid deposits were found in the wall of the submucosal blood vessels in the stomach, small and large intestine (Figure 4, 5 and 6). The pancreas was partially preserved, partially necrotic. The surrounding adipose tissue was necrotic with calcification and infiltrated by lymphocytes

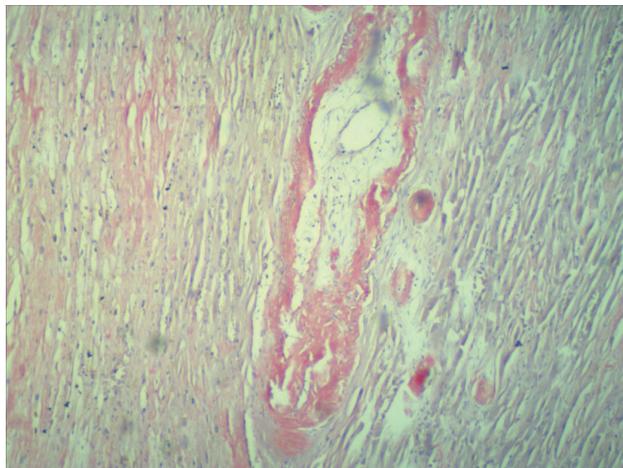


Fig. 1. Deposit of the amorphous eosinophilic material in wall of the heart blood vessels. HE 40x.

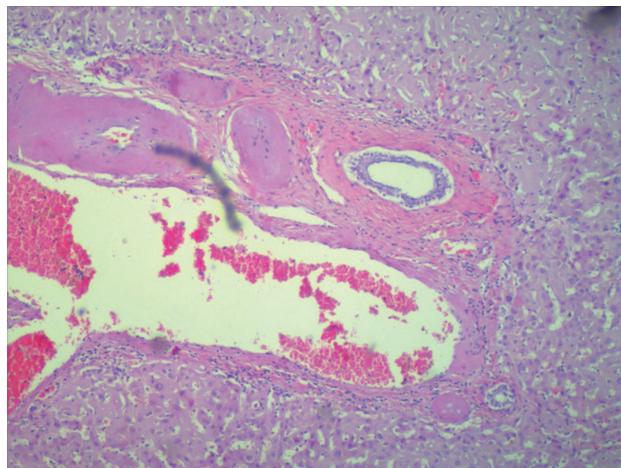


Fig. 3. Deposit of the amorphous eosinophilic material in wall of the liver blood vessels. HE 40x.

## Discussion

Amyloidosis is rare disease with incidence of approximately 6–10 case per milion persons a year. It is characterized by the extracellular deposition of abnormal fibrillar protein, which disrupts tissue structure and function. There are six types of amyloidosis: primary, secondary, hemodialysis-related, hereditary, senile and localized<sup>1</sup>.

The most commonly affected organs are the heart and kidneys while the GI tract is rarely affected, but this can occur in primary and secondary form of the amyloidosis. The amyloid deposits in the GI tract are associated with the diarrhea, anorexia, weight loss, nausea and vomiting, dyspepsia, hemorrhage, steatorrhea or constipation<sup>5,6</sup>.

Amyloid deposits in the stomach wall occur in less than 10% of patients. Endoscopic examination may show thickened gastric folds, gastric ulcers, hematomas, granular appering mucousa and plaque-like lesion. Histological

examination reveale amyloid deposition on the muscularis mucosa, submucosal vessels and muscularis propria in almost all areas of the gastric wall<sup>2–4</sup>.

Amyloid deposition in the GI tract is most prominent in the small intestine. Amyloid deposition is seen in the mucosa, the submucosal connective tissue, the muscularis mucosa, and muscularis propria, within nerves and mostly within blood vessel walls. With increased deposition, a variety of symptoms, such as bleeding, motility disorders, and malabsorption, may occur and deposition within blood vessel walls may lead to bowel ischemia, mucosal atrophy and ulceration, and eventually perforation<sup>2–6</sup>.

Amyloidosis of the large intestine must be differentiated from inflammatory bowel disease, ischemic colitis, malignant diseases and collagenopathies. The descending and rectosigmoid colon are mostly involved. Endoscopic examination may show polipous lesions, ulceration and

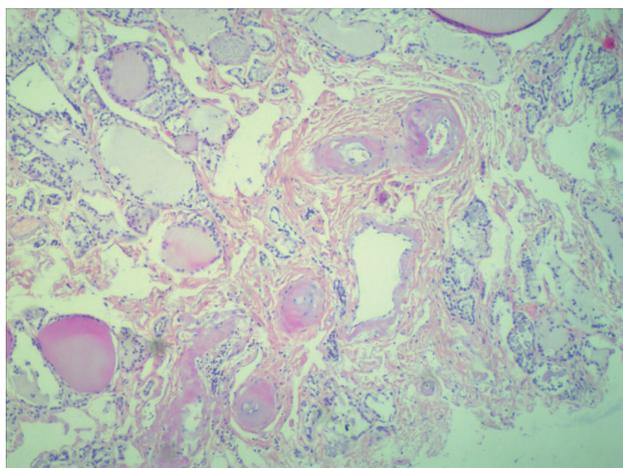


Fig. 2. Deposit of the amorphous eosinophilic material in wall of the thyroid gland blood vessels. HE 40x.

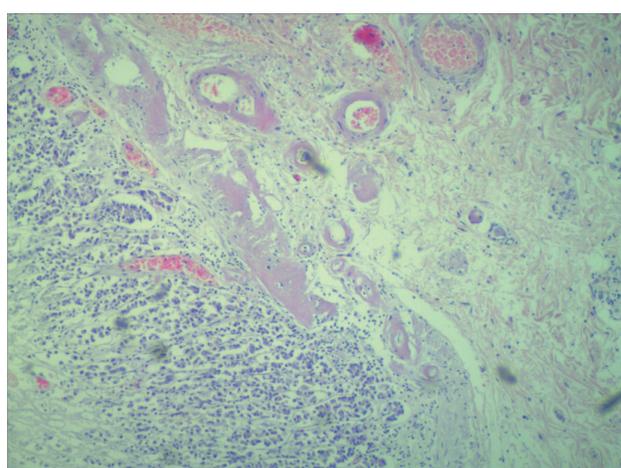


Fig. 4. Deposit of the amorphous eosinophilic material in wall of the stomach submucosal blood vessels. HE 40x.

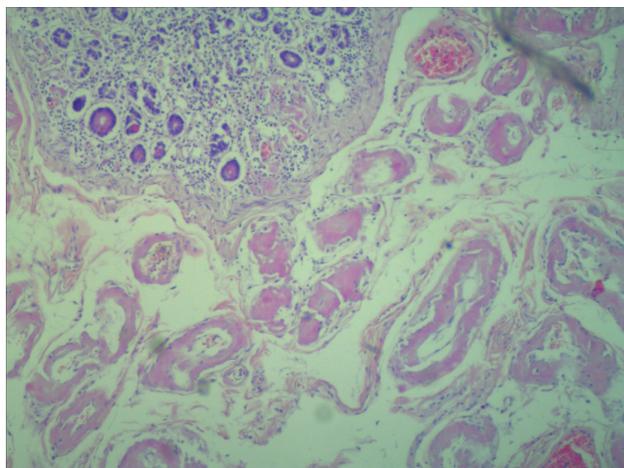


Fig. 5. Deposit of the amorphous eosinophilic material in wall of the small intestine submucosal blood vessels. HE 40x.

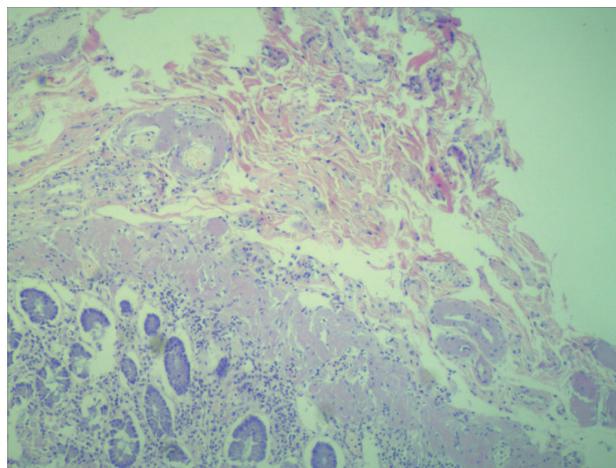


Fig. 6. Deposit of the amorphous eosinophilic material in wall of the large intestine submucosal blood vessels. HE 40x.

petechial lesions. The symptoms include motility disorders or pseudoobstruction, acute obstruction, rectal bleeding and colonic dilatation<sup>2,7</sup>.

In autopsy series, 56–95% of patients with amyloidosis had liver involvement. Clinical manifestations of hepatic amyloidosis are usually mild and included hepatomegaly with elevated alkaline phosphatase level, ascites which is often due to cardiac failure and hypoalbuminemia and hyperbilirubinemia. Disposal of amyloid is periportal, leads to atrophy of hepatocytes, and when blocking sinusoids, portal hypertension occurs. The safety of liver biopsies is controversial and bleeding is the most common complication.<sup>8</sup>

Cardiac amyloidosis is characterized by amyloid deposits in the ventricles and atria, perivascularly, as well as in the conductive system. The heart amyloidosis leads to infiltrative / restrictive cardiomyopathy. Amyloidosis of the

heart often coexists with significant dysfunction of other major organs and the presence of cardiac amyloidosis is often the worst prognostic factor<sup>9,10</sup>.

## Conclusion

In this article we presented the case of a patient who has been treated for a number of months by progressive heart failure and with non-specific symptoms by the GI tract. Clinical examination did not detect the cause of heart failure and progressive loss of weight and malnutrition. The patient died because of the multi-organ failure. The diagnosis of systemic amyloidosis was performed by examining samples obtained during autopsy. Systemic amyloidosis should be considered in patients with cardiomyopathy, proteinuria, hepatomegaly, and different and non-specific symptoms of GI tracts without specific endoscopic findings.

## REFERENCES

1. OBICI L, PERFETTI V, PALLADINI G, MORATTI R, MERLINI G, *Biochim Biophys Acta*, 1 (2005) 11. DOI: 10.1016/j.bbapap.2005.08.014.
2. LIM AY, LEE JH, JUNG KS, GWAG HB, KIM DH, KIM SJ, LEE GY, KIM JS, KIM HJ, LEE SY, LEE JE, JEON ES, KIM K, *Korean J Intern Med*, 30 (2015) 496. DOI: 10.3904/kjim.2015.30.4.496.
3. ISOMOTO H, KAMO Y, CHEN CC, NAKAO K, *Open Journal of Gastroenterology*, 2 (2012) 155. DOI: 10.4236/ojgas.2012.24030.
4. IIDA T, YAMANO H, NAKASE H, *J Gastroenterol Hepatol*, 33 (2018) 583. DOI: 10.1111/jgh.13996.
5. FONNESU C, GIOVINALE M, VERRECCHIA E, DE SOCIO G, CERQUAGLIA C, CURIGLIANO V, SORIANO A, OBICI L, GRIECO A, LAURIOLA L, GASBARRINI G, MANNA R, *Eur Rev Med Pharmacol Sci*, 1 (2009) 45.
6. GROISMAN GM, COHEN HI, *Case Rep Pathol*, 2014 (2014) 4. DOI:10.1155/2014/362835.
7. KYLE RA, GERTZ MA, LACY MQ, DISPENZIERI A, *Amyloid*, 1 (2003) 36.
8. PARK MA, MUELLER PS, KYLE RA, LARSON DR, PLEVAK MF, GERTZ MA, *Medicine (Baltimore)*, 82 (2003) 291. DOI: 10.1097/01.0000091183.93122.c7.
9. DESAI HV, ARONOW WS, PETERSON SJ, FRISHMAN WH, *Cardiol Rev*, 18 (2010):1. DOI: 10.1097/CRD.0b013e3181bba8f.
10. OMAR KS, RUBERG FL, *European Heart Journal*, 38 (2017) 1909. DOI: 10.1093/eurheartj/ehx210.

G. Stanić

Department of Pathology, Clinical Hospital »Sveti Duh« Zagreb, Ul. Sveti Duh 64, 10000, Zagreb, Croatia  
e-mail: gabrijela\_stanic@yahoo.com

## **NEOČEKIVANA SISTEMSKA AMILOIDOZA KOD BOLESNICE S RESTRIKTIVNOM KARDIOMIOPATIJOM:**

### **SAŽETAK**

Sistemska amiloidoza je rijetka bolest koju uzrokuje taloženje netopivih abnormalnih fibrilarnih proteina poznatih kao amiloid u izvanstaničnom prostoru. Proteinske naslage su komponente imunoglobulina koje proizvode plazmastanice i B-limfociti kao odgovor na antigensku stimulaciju. Razlikujemo tri osnovna oblika amiloidoze, primarni (AL), sekundarni (AA) i obiteljski oblik. Lokalizirani oblik amiloidoze javlja se u gušterači kod bolesnika s dijabetesom tipa 2 i kod pacijenata s kroničnom hemodijalizom. Klinička slika amiloidoze ovisi o zahvaćenim organima. Simptomi su nespecifični i uključuju umor, gubitak težine, nefrotski sindrom, restriktivnu kardiomiopatiju sa zadebljanjem interventrikularnog septuma i stjenke lijeve klijetke, periferne neuropatije, hepatomegaliju, makroglosiju, purpuru i dijatezu. U ovom radu prikazali smo neočekivani nalaz sistemske amiloidoze kod pacijentice s restriktivnom kardiomiopatijom i dispnejom, gubitkom apetita, kašljem i izraženom slabošću ali bez znakova malignih i hematoloških bolesti. Dijagnoza sistemske amiloidoze postavljena je na histološkim uzorcima nakon obdukcije.