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Case Report

# A Rare Case of Multiple and A Typical Plasmacytomas Locations - a

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## ABSTRACT

Solitary plasmacytoma can occure in the skeleton or in soft tissues. Multiple plasmacytomas are either primary or recurrent. We present the case of a 29-year-old patient hopspitalised for headache, dizziness, fever, dysphagia, olfactive disorders, swelling and pain of the left nasal region and left maxillary sinus. The CT scan diagnosed a tumor located at the nose and pharix, to which the hystopathological and immunohystochemical examination of biopsy established the diagnosis of extramedullary plasmacytoma of the nasal cavity, and ethmoidal and left maxillary sinus. At the time, he had no skeletal lesions. The patient postponed the suggested treatment. Six months later he returned and accepted the surgical excision, followed by radiotherapy. Then, it ruled out a possible multiple myeloma. Four months later he presented new lesions: an eight cm mass on the 6$^{th}$ right rib, osteolithic lesions on the posterior side of the T5 vertebra, on the left 5$^{th}$ rib, on the sternum, and macronodular lesions measuring 8 cm on the left lobe of the liver. The liver biopsy discovered an infiltrate with CD138 positive tumour cells. A repeated bone marrow biopsy showed again a normal marrow cellularity. He was treated with chemo- and radiotherapy and zoledronic acid.The relationship between plasmacytoma and the chronic hepatitis B infection and the diabetes is discussed. A careful monitoring and patient compliance are needed to an early diagnosis of possible new pasmocytoma lesions. A possible shift to a multiple myeloma should be constantly considered.


**Keywords:** Cholesterol; Hepatitis B; Liver; Nose; Plasmacytoma; Rib; Sinus

## INTRODUCTION

Plasmacytoma refers to a malignant plasma cell tumor growing within the axial skeleton or within the soft tissue [1]. The cells are identical to those seen in multiple myeloma, but they form discreet masses of cells in the skeleton or in soft tissues. The patients have no systemic disease [2]. International Myeloma Working Group defined three distinct groups of plasmacytoma: solitary plasmacytoma of the bone, extramedullary plasmacytoma and multiple plasmacytomas that are either primary or recurrent [1]. The most common of these is solitary plasmacytoma of the bone, accounting for 3-5% of all plasma cell malignancies [3]. Solitary plasmacytoma of the bones occurs as lytic lesions within the axial skeleton and extramedullary plasmacytomas most often occur in the upper respiratory tract (85%) but can occur in any soft tissue. Solitary bones and extramedullary plasmacytomas are mostly treated with radiotherapy, but surgery is also used in some cases of extramedullary plasmacytoma [4]. However, for estetic reasons the surgery is generally used when the lesions are not present within the head and neck region [5,6]. The skeletal forms frequently progress to multiple myeloma over the course of 2-4 years [4]. The word ”Plasmacytoma” is sometimes equated with ”plasma cell dyscrasia” or ”solitary myeloma” [7]. Plasmacytomas are a rare form of cancer. The median age at diagnosis for all plasmacytomas is 55. Both solitary plasmacytoma of the bone and extramedullary plasmacytomas are more prevalent in males, with a 2:1 male to female ratio for solitary plasmacytoma of the bone and a 3:1 ratio for extramedullary plasmacytoma [3].

## CASE REPORT

We present the case of a 29-year-old gypsy man who was admitted for: olfactive disorders, pain associated with the swelling of the nasal cavity and left maxillary sinus and epiphora. The patient’s mother had a history of type two diabetes (non-insulin dependent), and the patient himself also suffered of type two diabetes (non-insulin dependent) and has had an appendectomy. The patient currently lives with his mother, is unemployed, has an 8$^{th}$ grade level education and a hypercaloric diet. He is a smoker (10-15 cigarettes/day).

The 29-year-old patient presented to the Emergency Department of the Râmnicu Vâlcea County Hospital on June 07, 2014 with headache, dizziness, fever, dysphagia, olfactive disorders, swelling and pain of the left nasal region and left maxillary sinus. He also complained of intermittent epistaxis of the left nostril. The patient was diagnosed with a respiratory infection and acute tonsilitis, and the specialist in infectious diseases recommended treatment with antibiotics and anotorhinolaryngology consultation. A CT scan revealed opacification of the left maxillary sinus and of the left nostril, with a prolaps in the cavum as well as congestion of the right maxillary sinus. After these investigations, the patient was directed to an Otorhinolaryngology Clinic in Bucharest, where, on June 26, 2014 a nasal-pharyngeal tumor formation was excised. Initial examination raised suspicions of non-Hodgkins lymphoma, but a hystopathological examination and immunohystochemical tests confirmed a diagnosis of well-defined extramedullary plasmacytoma (a CD38 positive proliferation).

The patient was tested in the Hematology Clinic at Fundeni Hospital, Bucharest on August 11, 2014 where multiple myeloma was excluded, and the diagnosis of solitary plasmacytoma of the nasal cavity, ethmoidal and left maxillary sinus was confirmed. Radiological examinations revealed no skeletal lesions. The patient with grade 2 obesity, multiple tattoos received in unsanitary conditions, and with scarring resulting from suicidal self multilation on the forearms, was confirmed to suffer from type two diabetes and hepatitis B. It was recommended to the patient that he should undergo radiotherapy and seek a hepatologist, which the patient postponed.

On December 18, 2014 the patient was admitted to the Hematology Service of the Emergency County Clinical Hospital of Sibiu in a generally good condition, grade 2 obesity (BMI=39.2 kg/m$^2$), afebrile, and with healthy appetite. The patient presented with natural skin pigmentationfor his ethnic origin, multiple scars to the arms (self-inflicted), as well as multiple tattoos (located on the back of the thorax, right forearm and left upper-arm) and a presence of Celsius’ signs on the left nasal and sinus cavity. Upon palpation there was no evidence that the patient had adenopathy. The patient’s thorax was normally developed, with rale sounds in both lungs. He complained of pain on the right hemithorax when making sudden movements. His heart sounds were equipotent and equidistant, blood pressure was 130/70 mmHg,and pulse rate - 72/min. The patient’s abdomen was enlarged due to excessive adipose tissue and was not painful upon palpation; intestinal transit was normal. His liver was palpable at about 9 cm below the bottom rib, while the spleen could not be felt. Diuresis was within physiological limits. The patient was consciously and had bilateral reflexes.

The patient’s biological tests have shown: WBC=8.770/mm$^3$, HGB=16.1g/dl, PLT=181.000/mm$^3$, neutrophils=5.780/mm$^3$ lymphocytes=1.580/mm$^3$,monocytes=1.070/mm$^3$(200-1000/

mm$^3$),eosinophils=330/mm$^3$, basophils=10/mm$^3$; bilirubin=0.42 mg/dl, gamma glutamyl transferase=88 U/I (11-50 U/I), AST=20 U/L, ALT=25 U/L, serum urea=20 mg.dl, serum creatinine=0.81 mg/dl, cholesterolemia=135 mg/dl, glycemia: 201 mg/dl. Protein electrophoresis has shown: albumin=58%, alfa1-globulin=3.6%, alfa2-globulins=12.4%, beta1-globulins=8.4%, beta2-globulins=6.5%, gamma-globulins=10.6%, total proteins= 6.4 g/dl. The immune electrophoresis has shown: IgA=200 mg/dl, IgG: 700 mg/dl (below normal value), and IgM: 89.7 mg/dl. The patient's coagulation tests have been in normal values. A bone marrow biopsy excluded a multiple myeloma. The patient was detected positive for Hbs antigen and anti-HBc antibodies, and negative for Hbe antigen and anti-Hbe antibodies. DNA level of the Hepatitis B virus was 36 UI/mL (1.56 log/UI/mL); the detection limit was 15 UI/mL (1.18 log/UI/mL). All of the following tests were negative: anti-HDV and anti-HCV antibodies, HIV and VDRL. Due to the low-level of hepatitis B virus presence and normal level of transaminases, the patient was not eligible for an antiviral treatment. A cranial CT scan taken on May 18, 2015 showed right cerebellar sequelae of patchy ischemia, ischemic periventricular gaps, clouding of the left maxillary sinus and the left nasal fossa, with prolapse tumor in the cavum (Figure 1).

The patient proceeded with his radiotherapy treatment of the left nasal and ethmoidal cavity (total dose=45 Gy/25 parts/35 days) which the patient coped with quite well.For the associated pathology, the patient received: Silibinum 150 mg twice daily and Metformin 1000 mg twice daily.

The patient returned for a check-up four months later, witha generally good health, but with pain to the right thorax upon sudden movement. He presented with inflammatory syndrome and an x-ray of the right thorax revealed a homogenous mass of medium intensity measuring 5x2 cm attached to the 6$^{th}$ rib on the right side, whose antero-lateral arc was lysated. The patient's rib pain persisted and an ordered thoracic CT scan showed a voluminous mass measuring 8 cm on the 6$^{th}$ right rib, osteolithic lesions on the posterior side of the T5 vertebra and the left 5$^{th}$ rib. Osteolithic lesions were also present on the sternum, and macronodular lesions measuring 8 cm were present on the left lobe of the liver (Figure 2).

A repeated bone marrow biopsy showed again a normal marrow cellularity. An abdominal ultrasonographic examination performed on October 9, 2015 showed a global enlarged liver. A hypoechogenic tumoral mass measuring 8.5 x 6.5 cm with peripheral arterial vascularisation appeared on the 3$^{rd}$ segment of the left lobe (Figure 3), and the gall bladder was transonic.

The patient required a liver tumour biopsy, which was performed in Cluj on October 1, 2015. Four hepatic fragments were microscopically examined,in total of 11 mm long, with the presence of proliferation of malignant tumours and an excess of plasma cells dispersed in solid areas. The tumour cells were positive for CD138 and negative for LCA.AE1/AE3. The correlation between the hystopathological results and the immunohistochemistry in clinical context suggested a diagnosis of liver plasmacytoma.

The patient received the following course of treatment: chemotherapy (1 cycle of VAD therapy, followed by 6 cycles of bortezomib, dexamethasone and pegylated liposomal doxorubicin), a bisphosphonate (zoledronic acid - 4 mg/month, treatment which continues today), radiotherapy on the right ribs (total dose=50 Gy/25 parts/35 days), and supportive care, including hepatoprotection.

## DISCUSSION

The presenting patient is a young man (only 29 years old), with gigantic plasmacytomas having atypical locations: in the nasal cavity and liver. This diagnosis was a surprise to a so young patient. The nasal-pharyngeal tumor could be a pharyngeal carcinoma, as the patient is a smoker and cigarette smoke is involved in the occurrence of this type of cancer. Histopathological and immunohistochemical examination of the tumor estabilshed the diagnosis of plasmacytoma. It is noteworthy that the patient developed other 2 plasmacytomas in less than 1 year from the date of the initial diagnosis. The patient's coinfection with the hepatitis B virus raises the suspicion of viral implication in the appearance of hematological diseases, especially as the patient developed a third plasmacytoma, this time on the liver. However, there are no data on the possible implication of the hepatitis B virus in the of development or progression of plasmacytomas. A recent meta-analysis found an association between this infection and the risk of multiple myeloma only in sub-analyses which included high-quality studies and those with hospital-based control groups. Further studies are needed to confirm this possible association and to establish a possible pathogenetic mechanism [8].

Our patient's treatment was achieved with difficulty due to itssupressed immune system (by illness, aquiredumoral immune deficit, chemotherapy and radiotherapy) and during its chronic hepatitis B infection and the presence of diabetes (the patient's diabetes was also affected by corticotherapy). We also noted a patient's non-compliance with the treatment (he left the country right before the imagistic re-evaluation and of the suggested autologous peripheral stem-cell transplantation. The initial treatment was the surgical excision of the tumour, followed by radiotherapy, but when the patient developed multilocated plasmacytomas he was also subjected to chemotherapy.

We foundonlyone case of published liver plasmacytoma, appeared in a 77-year-old female who presented with lethargy, bilious vomiting, abdominal fullness and clay-colored stools. A liver guided biopsy showed a liver involvement byanatypical plasma cells infiltrate, with a nodular and sinusoidal pattern. Immunohistochemical tests identified the solitary extramedullary plasmacytoma [9].

A current issue for hematological medical research is the correlation between cholesterol disorders and hematological cancers. Recent studies showed that before treatment, the level of phospholipids and cholesterol in the blood was greatly reduced. After 3 or 6 cycles of chemotherapy, the quantity of lipids in the blood increased slowly to the limits of normal. It is known that cancerous cells use cholesterol for their own multiplication, and the level of cholesterol in these patients is low, and sometimes very low. An increase in the cholesterol levels during chemotherapy is a consequence of the response to the treatment and represents a marker of a favorable prognosis for these patients [10]. The evolution of patient's cholesterol levels before and after chemo- and radiotherapy for multiple plasmacytomas is presented in (Figure 4).

The patient presented low cholesterol levels at the first hospital admission (the lowest level was 72 mg/dl), as it can been seen in the figure. The cholesterol levels have increased after chemo- and radiotherapy, and could partially be a consequence of a favourable response to the treatment, and they are maintained in normal range until today. But we mention that the evolution of serum cholesterol levels in this casecould also be influenced by the treatment with

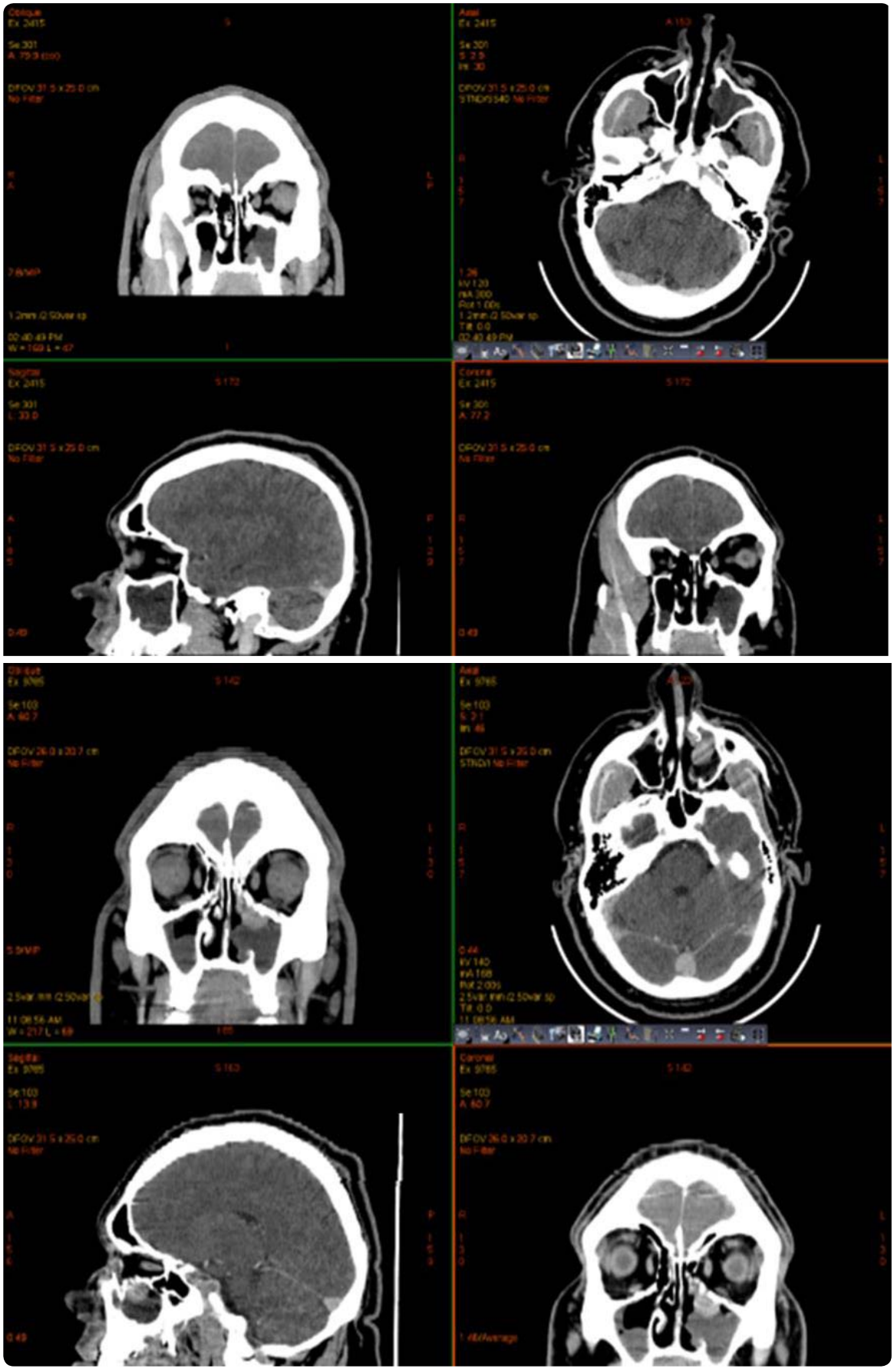

**Figure 1:** Cranial CT scan (May 18, 2015): clouding of the left maxillary sinus and the left nasal fossa with prolapse tumor in the cavum.

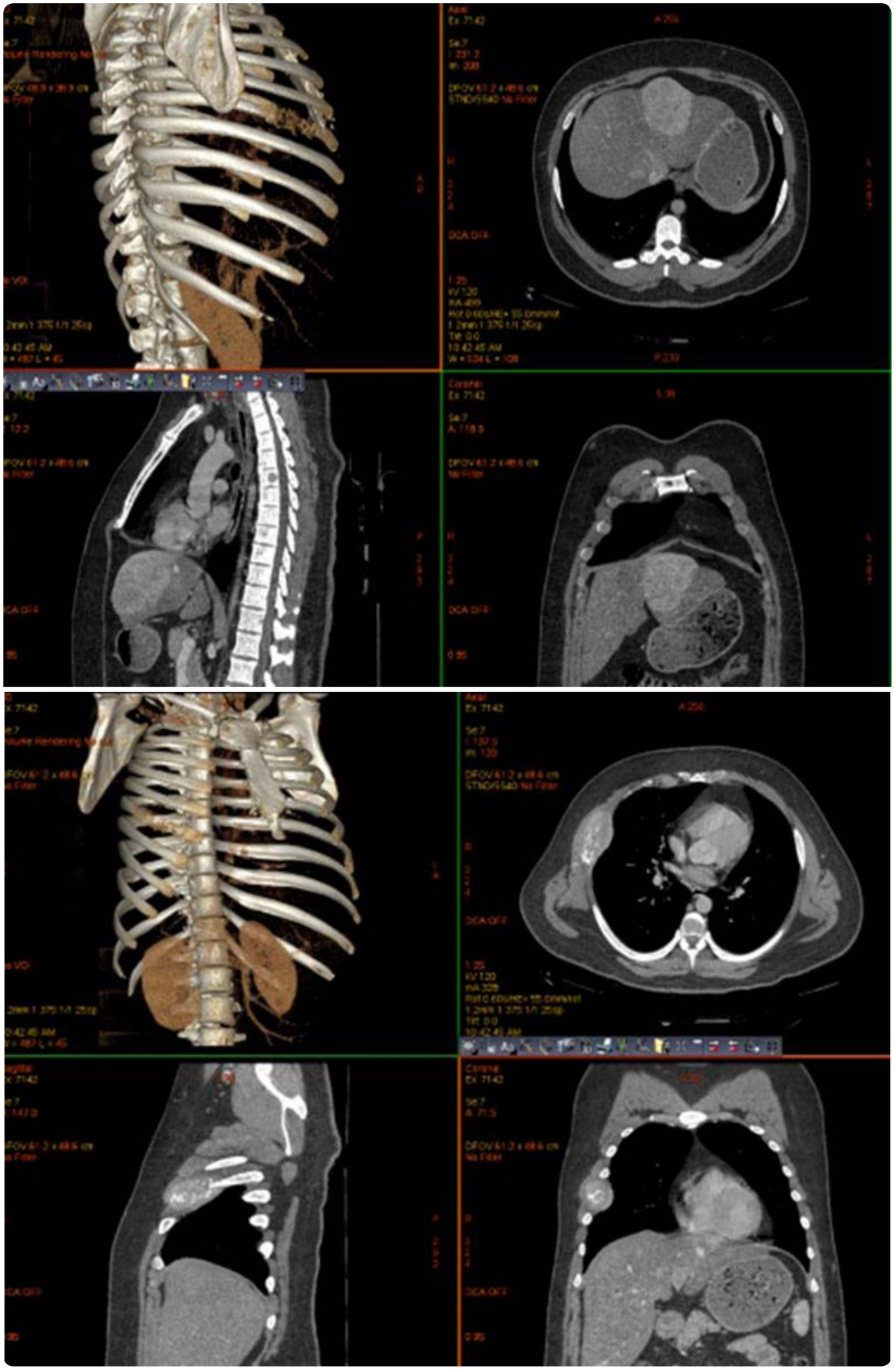

**Figure 2:** Thorax CT scan (May 30, 2015) has shown an osteolithic mass of the 6th rib, and macronodular lesions on the left lobe of the liver.

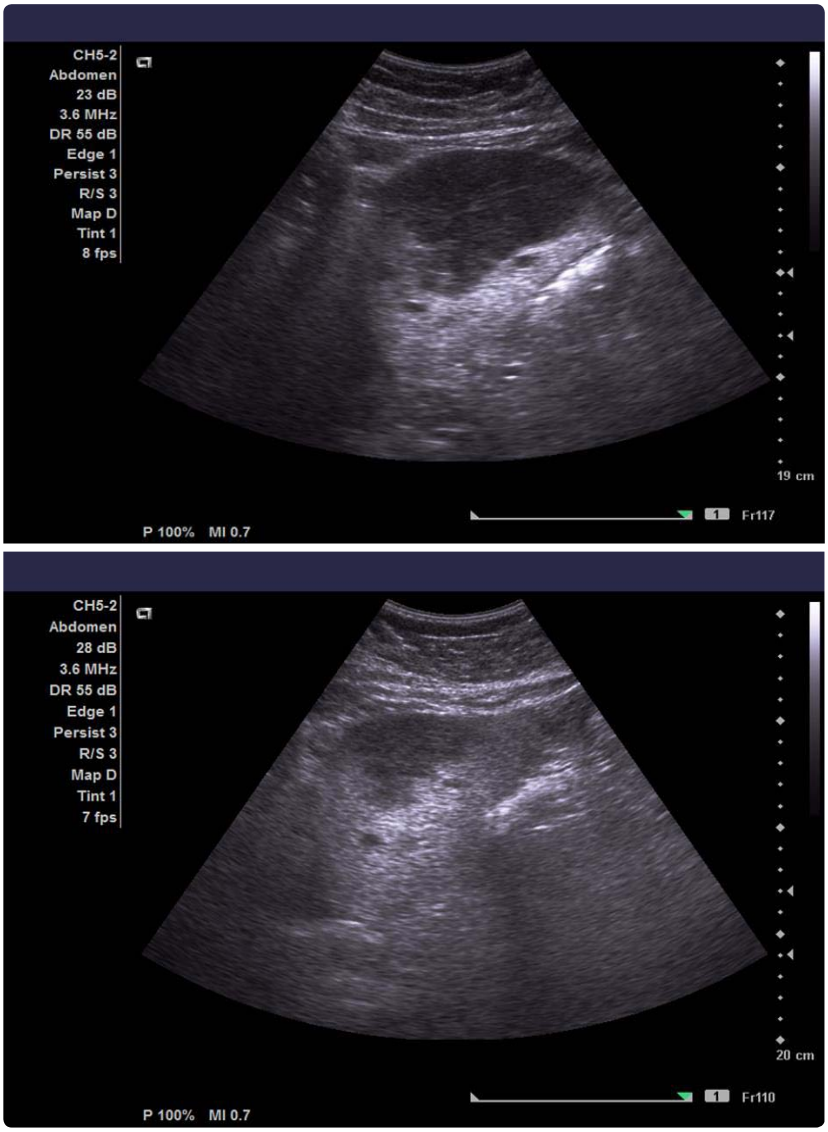


**Figure 3:** A hypoechogenic tumoral mass on the liver ultrasonographic examination.

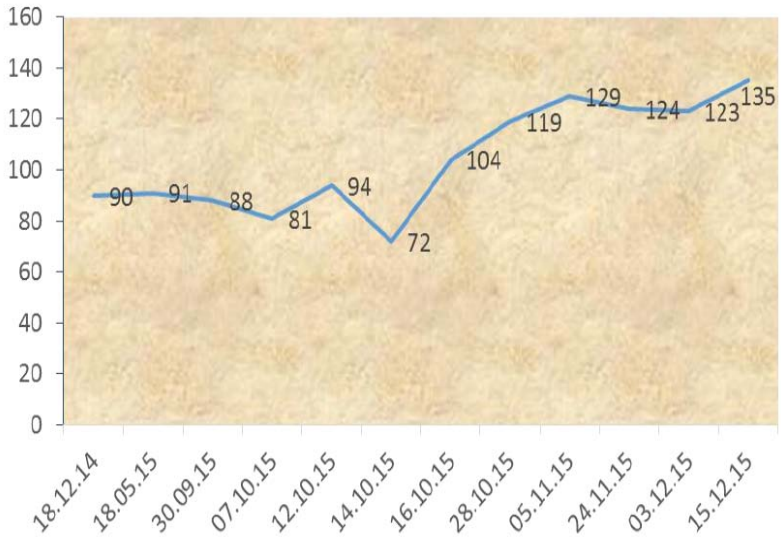


**Figure 4:** The evolution of patient's cholesterol levels.

zoledronic acid, which inhibits farnesyl diphosphate synthase, and which continues today.

However, it is difficult to estimate the prognosis of multiple plasmacytomas. Some studies have revealed that age, tumor size, site of origin (extramedullary versus bone), grade, M-protein and light chains, and radiotherapy dose influence the prognosis of these patients [11-15]. Further studies have found that light chain restriction is a prognostic factor [16,17]. About 50% of plasmacytomas progress to overt multiple myeloma in a 10-year follow-up, and 10% of them recur with a plasmacytoma [18]. The increasing use of CT scan, MRI and PET-CT in the evaluation of multiple plasmacytomas will eventually reveal multiple soft tissue lesions and perhaps additional bone lesions [19-21] and will establish in the future more adequate prognostic factors. For our patient, the long-term prognosis is doubtful.

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