Case No. 18

15-year-old female

Past medical history

The subject, a native of a southern Italian town, from early infancy experiences episodic attacks of anemia and jaundice. Growth and development are normal, even if marked by periodic episodes like those mentioned above.

Recent medical history

More recently, the symptomatology described above progressively increases for what concerns the frequency of attacks of anemia and jaundice, which with ever increasing intensity tend to become persistent for longer periods of time. Hospitalization c/o internal medicine divisions leads to the diagnosis of "hereditary nonspherocytic hemolytic anemia from erythrocyte pyruvate kinase (PK) deficiency". Blood transfusions become necessary at this point. Meanwhile, splenomegaly manifests itself and becomes increasingly more severe; painful fits start in the left hypochondriac region, with irradiation to the base of the thorax and to the left shoulder; jaundice is nearly constant and at times intense; pain in the right hypochondrium, which at times resembles hepatobiliary colic. The patient is hospitalized in the internal medicine ward, where all diagnostic tests are conducted that allow confirmation of the syndrome of nonspherocytic hemolytic anemia from erythrocyte PK deficiency and of interpretation of the worsening of the clinical picture as the result of episodes of splenic infarction and biliary lithiasis in the underlying congenital disorder. The patient is referred to our ward with this diagnosis.

Physical examination

The patient is in very poor conditions and jaundiced. Examination of the thorax reveals a raised base of the left lung with little expansion on inspiration. The abdomen is tractable. The spleen is palpable, clearly enlarged (megalic) with the pole below the umbilical transverse line, and presents a sustained firmness; surface irregularities are also seemingly discernable. Liver is normal. Pain in the right subcostal region; positive Murphy's sign.

Noteworthy among the results of **blood tests** taken during previous hospitalizations are: moderate anemia, reticulocytosis, decreased level of α2-globulin (haptoglobin), increase in indirect bilirubin and confirmation erythrocyte PK deficiency; HCV positive.

Chest X-ray (Fig. no. 1) confirms the raised left dome of the diaphragm.

CT scan (Fig.s no. 2 - 3) shows enlarged, irregularly shaped spleen; gallbladder lithiasis.

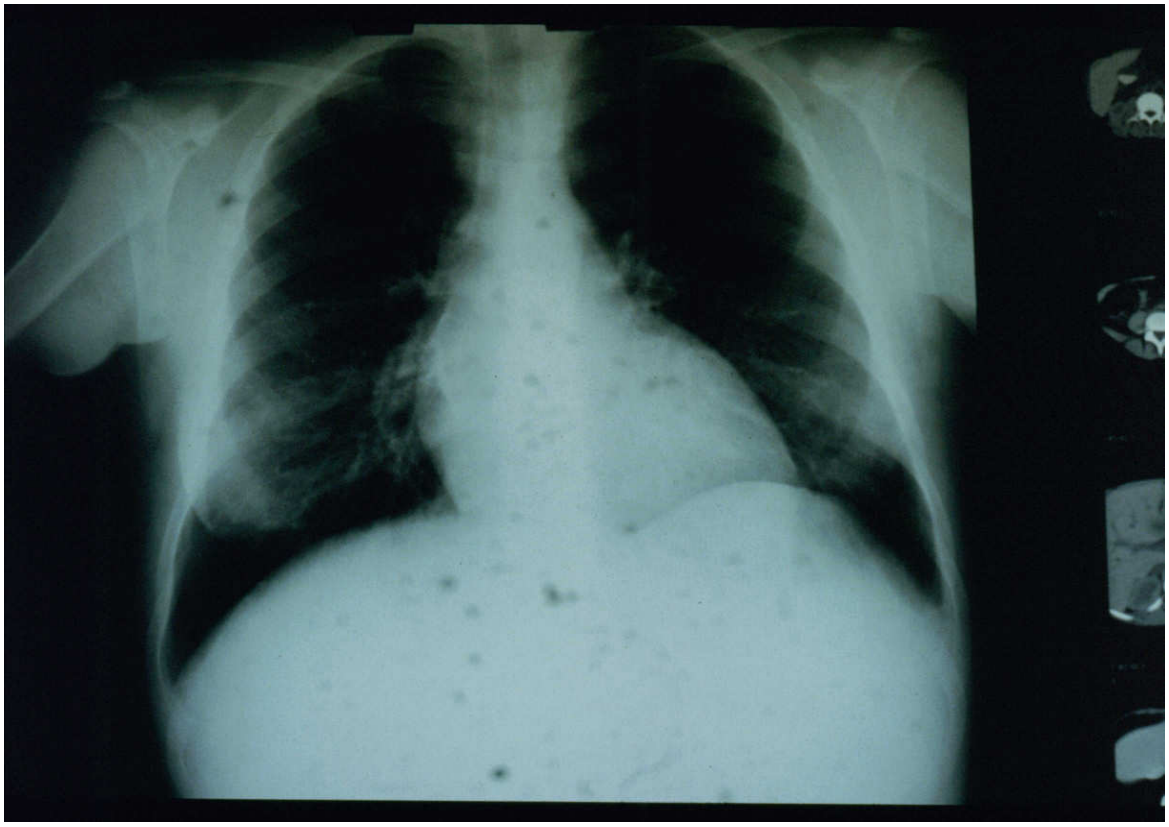

Fig. 1

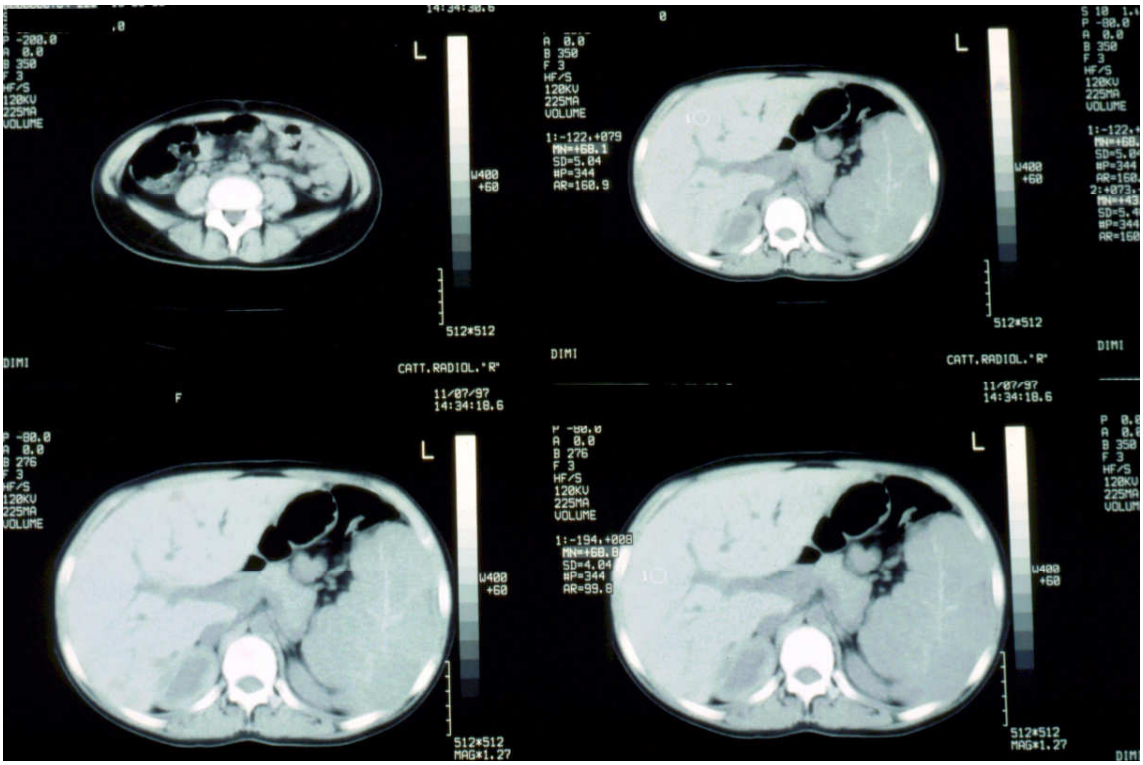
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Fig. 2

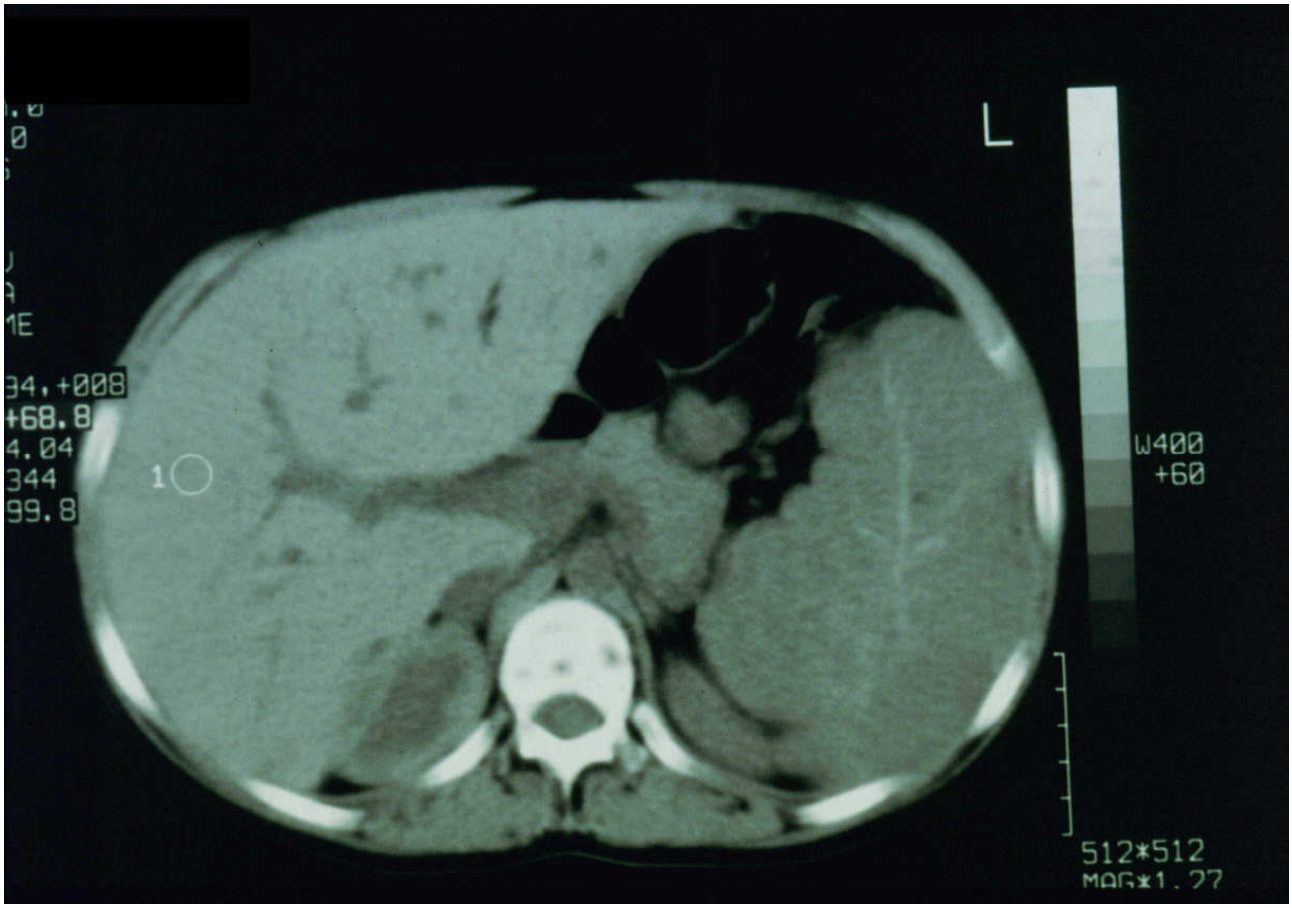

Fig. 3

In agreement with the internal medicine specialists, splenectomy and cholecystectomy are planned.

Operation

Xipho-subumbilical median laparotomy revealing a voluminous, multilobed spleen, with perisplenitis and strong adhesions to the left colic flexure, to the gastrocolic ligament and to the diaphragm. Opening of the epiploic retrocavity and skeletonization of the greater curvature of the stomach down to the short gastric vessels. Isolation of the splenic artery to the celiac trunk, where it is tied. Large collateral venous circles from the splenic hilum, the gastrocolic ligament and the pancreas are interrupted. The tail of the pancreas is united to the splenic hilum with such a strong adherence that its isolation is dangerous. Thus, interruption of the tail of the pancreas and splenic hilum elements with a GIA 70 stapler is preferred. Nearly half of the splenic mass is lodged in the left hemidiaphragm, which is elevated, and this portion of the spleen is separated from the rest of the organ by a serous diaphragm. To detach the spleen from the diaphragm, the triangular ligament of the left hepatic lobe is interrupted and the above-mentioned serous diaphragm is carefully interrupted (so as not to damage the diaphragm) with bipolar scissors until the anterosuperior portion if the spleen is freed. Isolation of the posterior part of spleen from the kidney and adrenal gland is also difficult. The spleen, shrinkinking in volume in the meantime, is extracted. Hemostasis of the residual space. The gallbladder is full of stones, the common bile duct is normal, the cystic duct small. Isolation of Calot's triangle. Transcystic cholangiomanometry-graphy reveals intrabiliary pressure within normal limits and the correct flow of bile into the duodenum; bile ducts show no lithiasic content. Interruption of the artery and the cystic duct. Retrograde cholecystectomy.

Toilette of the abdominal cavity. Tubular drainage of the left subdiaphragmatic region. Suture of the abdominal wall.

Pathologic anatomy

Macroscopic: the spleen weighs 800 grams, and presents a surface deformed by countless pits that divide it into lobes (Fig.s 4 - 5). It is suspected that these features are the result of numerous infarctive events, with the retraction of subsequent cicatricial outcomes.

On opening, the gallbladder is loaded with numerous black stones, each only a few millimeters in diameter, thus giving them a so-called *caviar-like appearance* (Fig. 6).

Microscopy confirms the cicatricial nature of above mentioned morphological features.

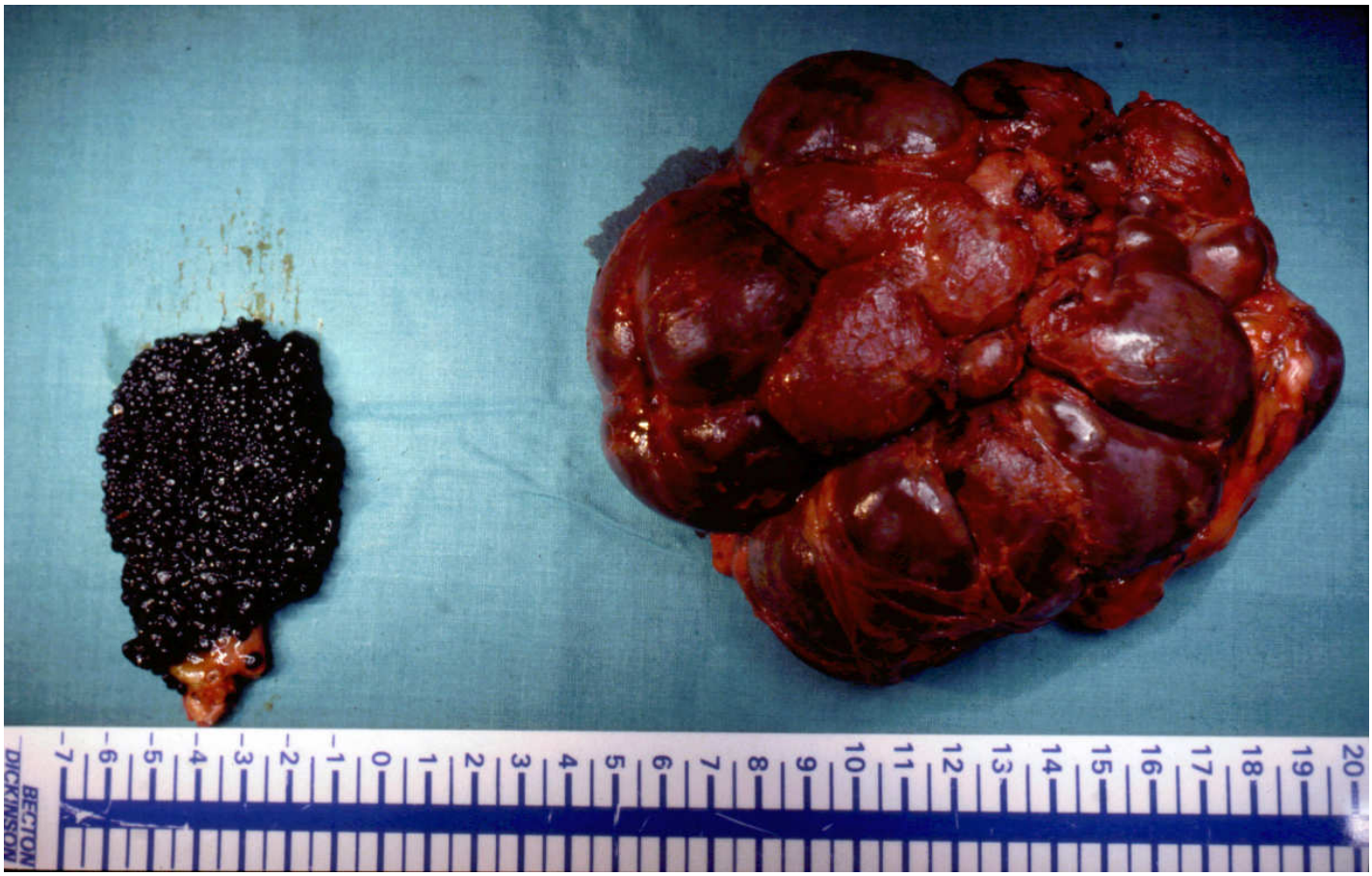

Fig. 4

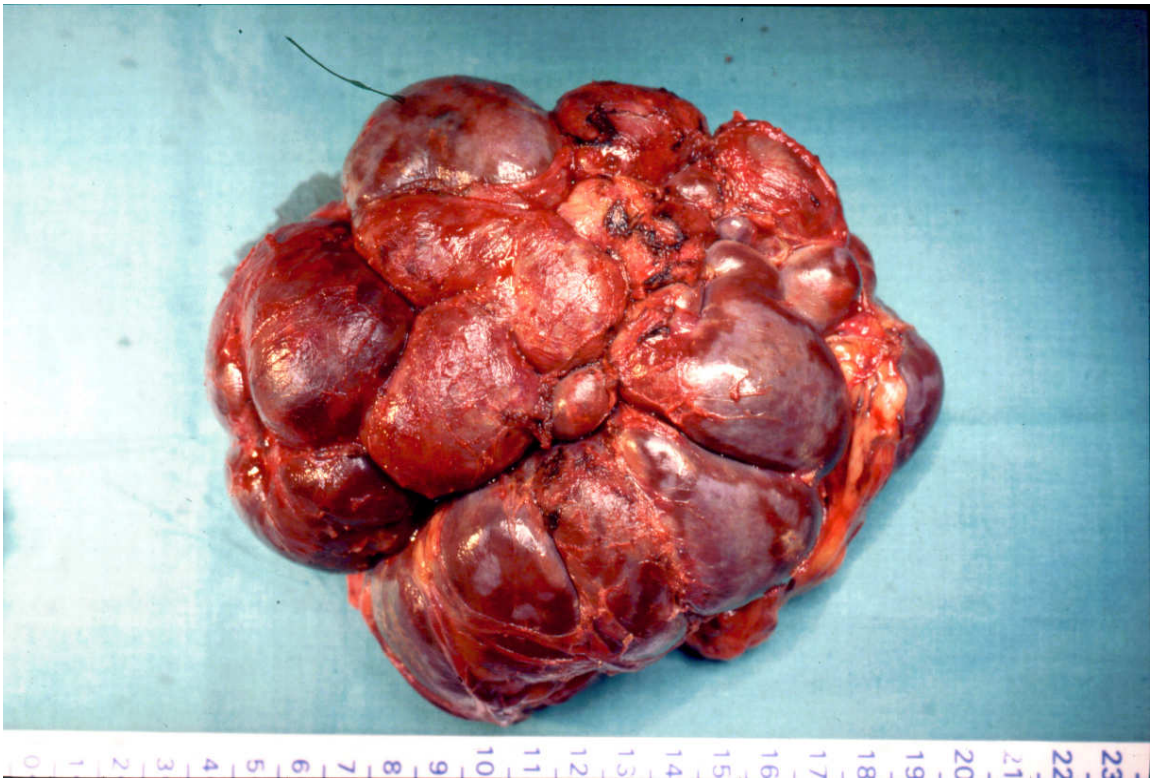

Fig. 5

Fig. 6

Postoperative course

Regular and uneventful. On the third day, because drainage was negative, the tube placed in left subdiaphragmatic region was removed. However, the patient developed high fever after approximately 48 hours. Ultrasonography (US) of the abdomen reveals a collection in the residual splenic space. US-guided tubular drainage is positioned and allows evacuation of the purulent accumulation.. Drainage and targeted antibiotic therapy achieve complete resolution of the complication after a few days.

The patient, whose conditions are considerably improved, is entrusted again to her original attending physicians for follow up and treatment of the underlying hematological disease.

Remarks

The clinical case described above regards a young female patient, a 15-year-old girl, whom since early infancy had been afflicted with fits of jaundice and anemia. These phenomena became increasingly more pronounced with time, and more recently splenomegaly and episodic abdominal pain appear, at intervals in the left hypochondrium, at others in the right: in this latter case, the pain sometimes mimics hepatic-biliary colic.

When the patient came under our observation were able to establish noteworthy enlargement of the spleen, which on physical and radiological examinations presented an irregular surface. These findings, together with the overall clinical pictures and the painful fits, prompted the hypothesis of previous and repeated events of splenic infarction. In parallel, imaging tests confirmed that clinical presumption of cholelithiasis.

As we've seen, this clinical picture fits very well with the syndrome of hereditary nonspherocytic hemolytic anemia from erythrocyte pyruvate kinase (PK) deficiency, a recessive autosomal disease from mutations in the PKRL gene. Metabolic anomalies ensue, such as depletions of ATP, high levels of 2,3-diphosphoglycerate, and inefficient anaerobic glycolysis.

The pathologic manifestations, such as neonatal jaundice, even if of varying intensity, are already present at birth. The symptomatology may worsen with age, as in our case. The increase in intensity of chronic hemolysis and the anemia that follows leads at a certain point to the need for blood transfusions. The spleen plays an important role because it is where PK deficient erythrocytes, particularly reticulocytes, are sequestered, thereby resulting in hemolysis, the increase in serum unconjugated bilirubin, jaundice, and the formation of pigment gallstones. Such intense activity over time leads to enlargement of the organ. Some authors have reported thrombotic vascular phenomena from persistent thrombocytosis: events of this kind may well explain the picture of splenic infarction seen in our patient.

All of these elements thus seem to help us predicate a pathogenetic interpretation of the clinical and anatomo-pathological features of the case. And, in final analysis, it is precisely these latter that from a surgical standpoint are of most interest. This said, of course, without minimizing the importance of the underlying hematological disorder, which remains classified among "rare diseases", with a very low prevalence in the general Caucasian population (with rates varying from study to study: 1/20,000; 51/1,000,000; 3/1,000,000; etc.).

In fact, splenectomy is generally not difficult, even when the organ is quite enlarged (as we have often encountered). In this case, however, surgery proved to be problematic because of the serious episodes of perisplenitis that had generated the strong adhesions of the perisplenium to adjacent

structures. Another finding that was entirely unexpected - unique, rather, even in our extensive experience in surgery of the spleen - was the organ's appearance: irregular due to the presence of multiple lobes, which led us to define this feature as *cerebriform*.

The anatomo-pathological study of the organ revealed, as was predictable, that this deformation was the result of multiple infarctions, which also accounted for such intense perisplenitic processes (Fig.7).

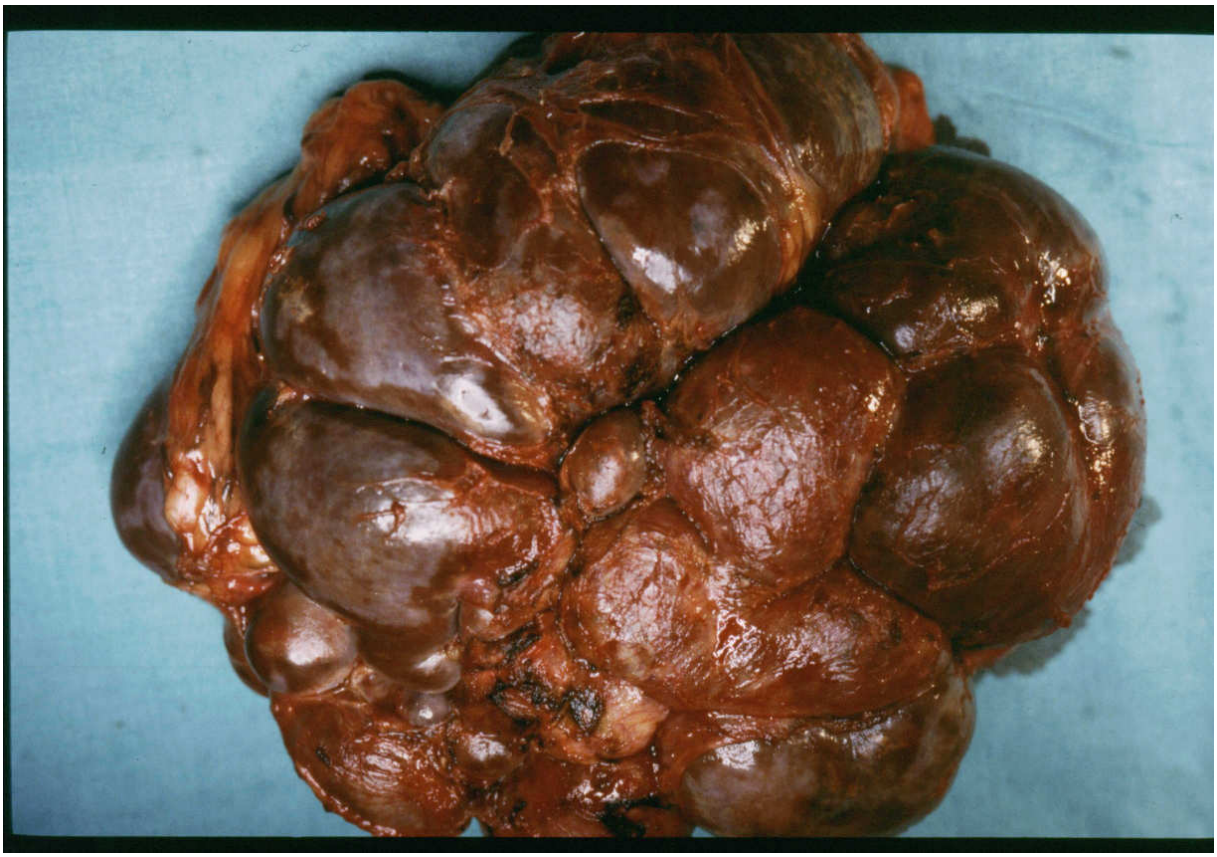

Fig. 7

And still one more, "picturesque" finding: the *caviar-like* appearance (Fig. 6) of the gallbladder's lithiasic contents. It is well known that hemolytic diseases, especially those occurring in neonates and in early infancy, often induce biliary pigment lithiasis, even in the common bile duct, but this was a feature that we, at least, had never encountered.

It is for this surgical and anatomo-pathological peculiarity that we believed this case worthy of attention and discussion.
