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Evolution of alveolar echinococcosis of the liver: new approach by CT imaging

M Claudon[1], A Gérard[2], D Régent[1], M Bessières[1], L Bresler[3], B Hoen[2] and B Champigneulles[4]

A retrospective analysis of CT findings in 20 patients failed to confirm the usually poor prognosis of hepatic alveolar echinococcosis: 13 cases showed total stability or only slight internal changes (follow-up: m = 4 years); regression was noted in 2 necrotic lesions. In 4 cases (20%), CT demonstrated a progressive increase in lesion dimensions, due either to parasitic growth or to development of necrosis; lesion-doubling time was very long (m = 37 months). The main CT signs (size, calcifications, necrosis) have no value in prognosis. The lack of correlation between clinical or biological data and radiologic findings justifies a periodic survey by CT. Medical treatment with Imidazole seemed to be efficacious in several cases but its exact role was difficult to determine because of the spontaneous and unpredictable evolution of the parasitosis.

Key words : Liver — Echinococcosis — CT — Calcification — Abscess

Alveolar echinococcosis is a human parasitic infection caused by the larval form of Echinococcus multilocularis. Its endemic area is wide, involving most of the temperate regions of the northern hemisphere. The infection spreads via the digestive tract and creates a primary source of infection in the liver. Parasitic growth occurs — in a different manner than that of the hydatid cyst — by external encystment, accompanied by a marked fibro-inflammatory reaction, which produces a slowly growing pseudo-tumoral process; macroscopic studies show a preferential involvement of the hepatic venous system along the portal axis to the level of the hilum, sometimes with local extrahepatic extension. Lesion necrosis and calcification are frequent; distant metastases (lung, brain, bone) may also occur [1-4]. Most published studies [5-9] note the spontaneous, unpredictable, and inevitable evolution leading to death in 52 to 70% cases [6-7]. However, some nonprogressive or even spontaneously regressing cases have been reported [2, 3, 10], which modify a negative overall impression which has not, in fact, been justified by any longitudinal study.

The Lorraine region is one of the main endemic areas of alveolar echinococcosis in France. The patients detected in our hospital have undergone strict clinical, biological, and radiologic follow-up for ten years. This represents a large retrospective population which allows observation of various evolutionary features and confirmation of the importance of imaging in the follow-up of this parasitic infection.

Material and methods

Among all patients followed in our hospital, 20 patients in whom serial scanning had been performed over at least 2.5 years were selected. There were 12 women and 8 men aged between 24 and 72 years (average = 54 years); in all cases, the diagnosis was proved with biopsy and/or serology.

In 16 of 20 cases, the disease was suggested by common clinical signs (pains in the right hypochondrium, fever, mild alteration of general well-being, hepatomegaly, diarrhea); only 4 of these 16 patients presented with jaundice or subclinical jaundice; 3 cases were diagnosed in the course of biological or ultrasound evaluation performed for another reason; a spinal involvement was revealing in the remaining case.

The radiologic evaluation initially performed (AFP, US, CT ± angiography) showed the following characteristics:

- *number of lesions:* only 1 site of infection in 11 cases, 2 sites of infection in 6 cases, 3 in 3 cases; a total of 32 sites of parasitic infection;
- *site:* right lobe of liver predominating in 18 lesions, left lobe in 14 lesions;
- *size:* from 1.5 to 18 cm with an average size of 6.6 cm;
- *type:* (according to the CT description in 11) 10 lesions appeared as an early homogeneous form, hypoechogenic on US and hypodense on CT; 12 lesions associated with areas of central necrosis and regions of microcalcifications, a "typical" appearance; 5 lesions were massively necrotic and 5 others were massively calcified;
- *complications:* 3 cases were accompanied by dilatation of the intrahepatic bile ducts; 1 case had pericardial effusion as a result of transdiaphragmatic extension; extra-hepatic retrohilar development was observed in 1 case; and 2 patients presented with spinal or secondary pulmonary symptoms.

Four patients initially underwent surgery, removing all lesions or only a part single (right hepatectomy: 1, left hepatectomy: 1, partial resection: 1, enterocolic anastomosis: 1); 1 patient underwent curative left hepatectomy 2.5 years after diagnosis, during a laparotomy performed because of complications due to gallstones. All patients underwent treatment with Imidazole (Flubendazole until 1983, Albendazole from 1983 to 1986, Mebendazole since 1986) on a continuous or discontinuous basis; clinical, ultrasonographic, and biological follow-up (HCT, hepatic and immunologic evaluation) was performed every 3 months, or 6 months in stable cases; CT follow-up (Tomoscan 310 Philips; sections performed

[1] Département de Radiologie, [2] Département de Maladies Infectieuses, [3] Service de Chirurgie C, [4] Service d'Hépato-Gastro-Entérologie, CHU de Nancy, Hôpital de Brabois, RN 74, 54500 Vandœuvre-lès-Nancy, France

Offprint requests: M Claudon

before and after intravenous injection of iodinated contrast) was performed every 6 months or once a year in stable cases. The follow-up was from 2.5 to 7 years with an average of 4.5 years.

The CT results were reviewed, analyzed, and compared a second time to the clinical and biological observations of the same period.

Results

Radiologic evolution

Several evolutionary features were observed:

A. *Regression* (Fig. 1). In 2 patients (10%) who presented with the massively necrotic form and follow-up of 3 to 8 years (average = 5.5 years), an objective regression of their lesions occurred (from 5 to 2 cm in 1 case and from 8 to 4 cm in the other case, which also was associated with massive calcifications).

B. *Total stability*. In 5 patients (25%), with follow-up over 2.5 to 5.5 years (average = 3.6 years), no change in the size or appearance of the lesions occurred. Evaluation of the lesion characteristics revealed that they frequently contained massive calcifications (55%) and that most of them were small (average = 4.5 cm).

C. *Slight internal modifications* (Figs. 2, 3). In 8 patients (40%), with a follow-up of 3 to 5.8 years (average =4.7 years), the size of the lesions did not vary, but moderate variability of their constituent features were noted, mainly an increase of peripheral calcification and rarely an increase in necrosis. The distribution according to the morphological type and size was not different from the general population.

D. *Complications*. Five patients (25%), followed for a period of 3 to 6.5 years (average = 4.3 years) had radiologic complications: one developed portal hypertension due to a fibrous compression of the portal bifurcation during regression of an infectious focus; the 4 remaining patients developed progressive increase in the size of the infectious site which led to consideration of surgical resection or transplantation.

The lesion growth occurred because of 2 major factors:

- *Parasitic growth:* in 1 patient (Fig. 4 A), the lesion growth was slow (transverse diameter increasing from 5 to 7.5 cm in 6 years, i.e. an average doubling time of 42 months). The growth was regular, peripherally located, and tended towards the hilum which could be involved in 10 to 15 years, according to the rate of growth. The initial site of parasitic infection was very homogeneous, uniformly hypoechogenic on US, and hypodense on CT. Internal alterations later changed its appearance: dense calcifications appeared between 2 consecutive follow-ups, manifest by peripheral micro-calcifications which were surrounded by an external rim of parasitic tissue from which the growth continued; regions of necrosis subsequently appeared and remained small.

- *Increase in necrosis:* in 3 other patients, the lesions increased in size more rapidly (mass increase from a mean of 12 to 17 cm in 4 years, i.e. an average doubling time of 33 months) (Fig. 5). There was a definite growth of tumor tissue, but the development of massive central necrosis seemed to be the main factor in the increased size at the infection site. Hepatomegaly was palpable in the iliac fossa. In these more rapidly evolving forms, the calcium depositions often changed, increasing, regressing, and sometimes reappearing later in a marked fashion. The increase of the lesion size in our 4 patients did not produce obstructive jaundice, portal hypertension or signs of extrahepatic localization. In one case which became massively necrotic, an enteric fistula was suspected because of the presence of gas (Fig. 5) within the necrosis, but this was never directly confirmed.

Clinical and biological correlations

A comparative analysis of the CT results and of the clinical and biological follow-up showed:

- excellent radiologic correlation in stable or regressive forms, for which the clinical prognosis was excellent and the laboratory features were normal;
- satisfactory correlation in the forms presenting only with internal variability: the majority of the patients did not present with clinical complaint or biological abnormality; 1 patient complained of epigastric pain which seemed minor considering the marked hepatomegaly; 3 patients (37%) presented with multiple episodes of icterus or cholestasis which was related to a slight dilatation of the intrahepatic biliary ducts on CT; in all cases, these episodes regressed, but sometimes recurred;
- discordance in the 5 progressive cases because 2 patients did not present with clinical or biological complaints; 2 patients had minor clinical complaints of epigastric or hypochondral pain. The biological findings in the 4 first patients were not significantly abnormal. Only 1 patient presented with systemic signs with diminished well-being, continuous pain, weight loss, exacerbation of an inflammatory syndrome, and abnormal liver function tests.

Discussion

Evolutionary features

This study contradicts the generally held concept that alveolar echinococcosis is associated with a poor and oftentimes fatal prognosis. The study confirms the slow evolution usually noted in this disease and also documents several evolutionary features:

A. *Most forms are stable (25%) or demonstrate minor variability (40%)*, as seen in 2/3 of the cases, with an average follow-up of more than 4 years: stability is seen in massively calcified forms, especially if they are involuted; however, this stability is also noted in other types of lesions regardless of the degree of intrahepatic extension. It is particularly striking how some large lesions which obliterate the hilum do not progress over time. This finding must lead to caution with regard to future surgery. It is not possible to assume recovery even if the lesion is massively calcified and involuted: in 1 case, where resection was performed, the pathologic examination showed persistent parasitic elements.

B. *Possibility of regression of the site of parasitic infection:* 10% of the lesions show objective regression even

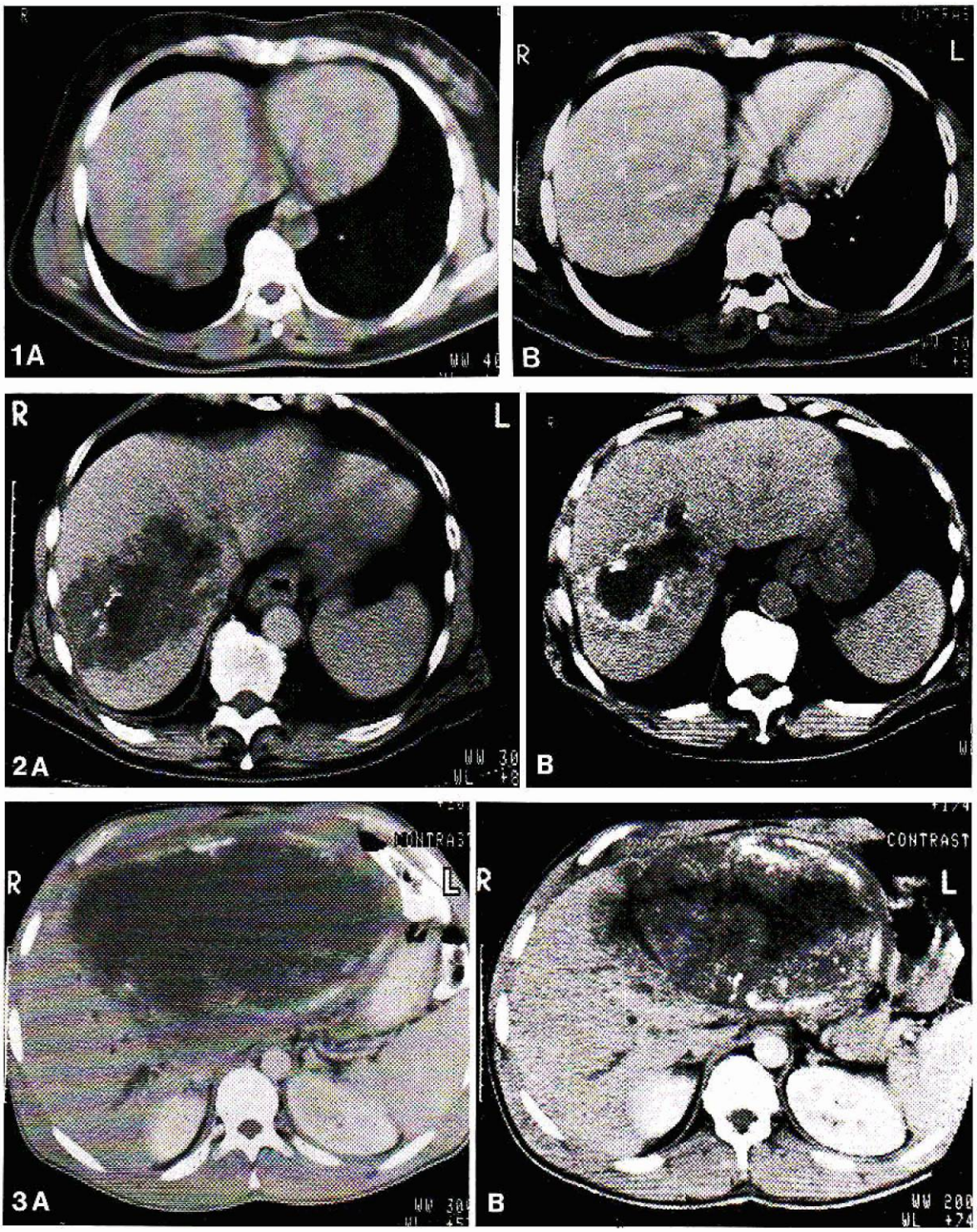

Fig. 1. **A** *1985:* predominantly necrotic mass in segment VII in subphrenic location (Ø 4 cm);**B** *1988:* clear decrease in size

Fig. 2. **A** *1985:* hypodense mass in the dome of the liver with rare calcifications and a small central zone of necrosis; peripheral extension into the normal parenchyma: **B** *1989:* clinically stable; no noticeable variation in the size of the lesion which is significantly calcified and has extensive regions of necrosis

Fig. 3 A, B. Massively necrotic form in the left lobe, with hilar extension. **A** *1985:* mucocutaneous icterus. Marked dilatation of the right intrahepatic biliary ducts. **B** *1988:* disappearance of the icterus: alkaline phosphatase slightly elevated. Increased calcification within the parasitic mass. Moderate regression of the dilatation of the intrahepatic biliary ducts

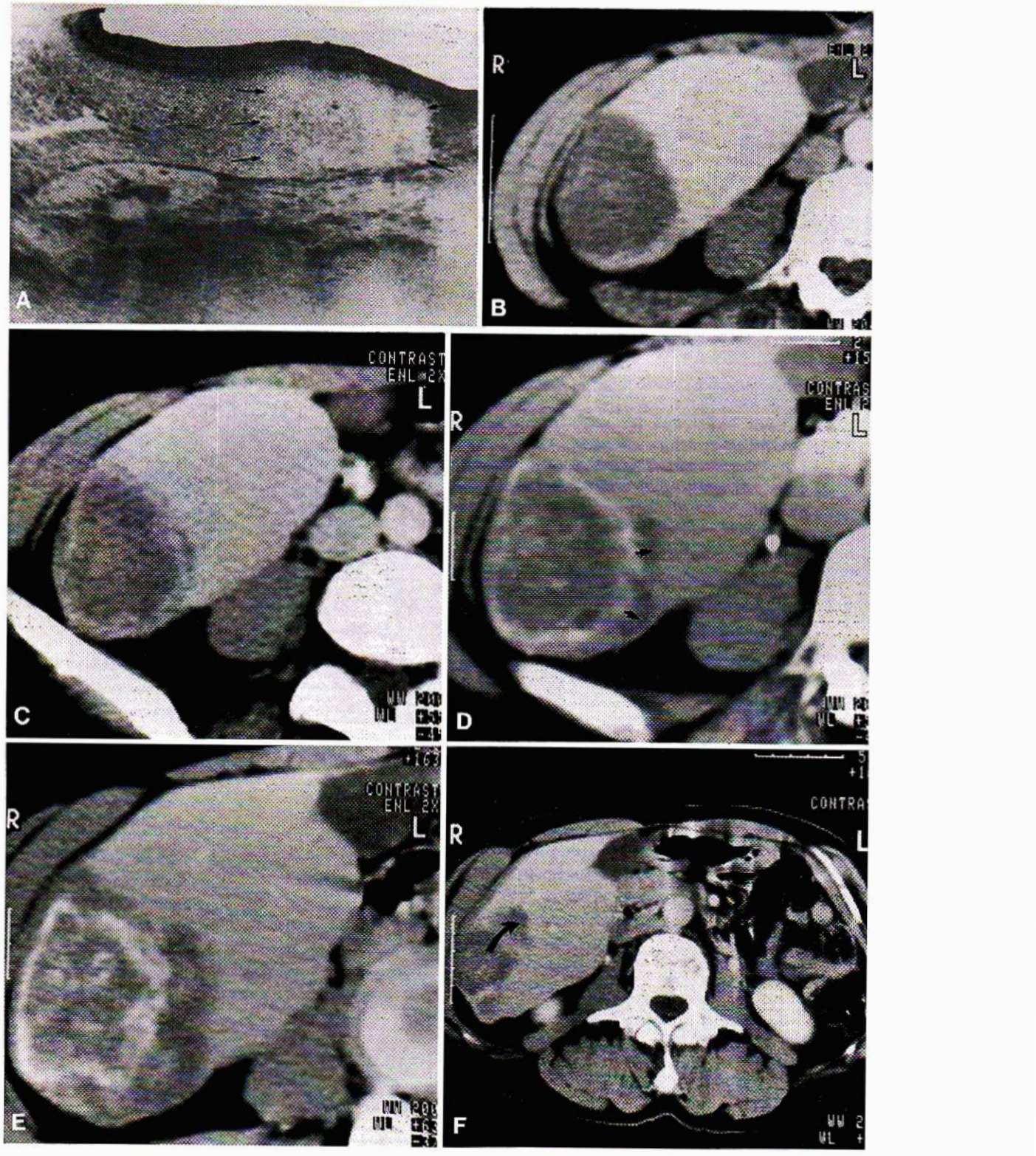

Fig. 4. *1982:* **A** US (= longitudinal section) = initially homogeneous form (→); **B** post-contrast CT sections passing through the centre of the lesion.
1983: **C** presence of a double peripheral border
1984: **D** appearance of a peripheral rim of microcalcifications, but continuation of external parasitic growth (→)
1988: **E, F** continuation of the parasitic growth, with 2 superior extensions *(F)* one of which is oriented towards the hilum (→)

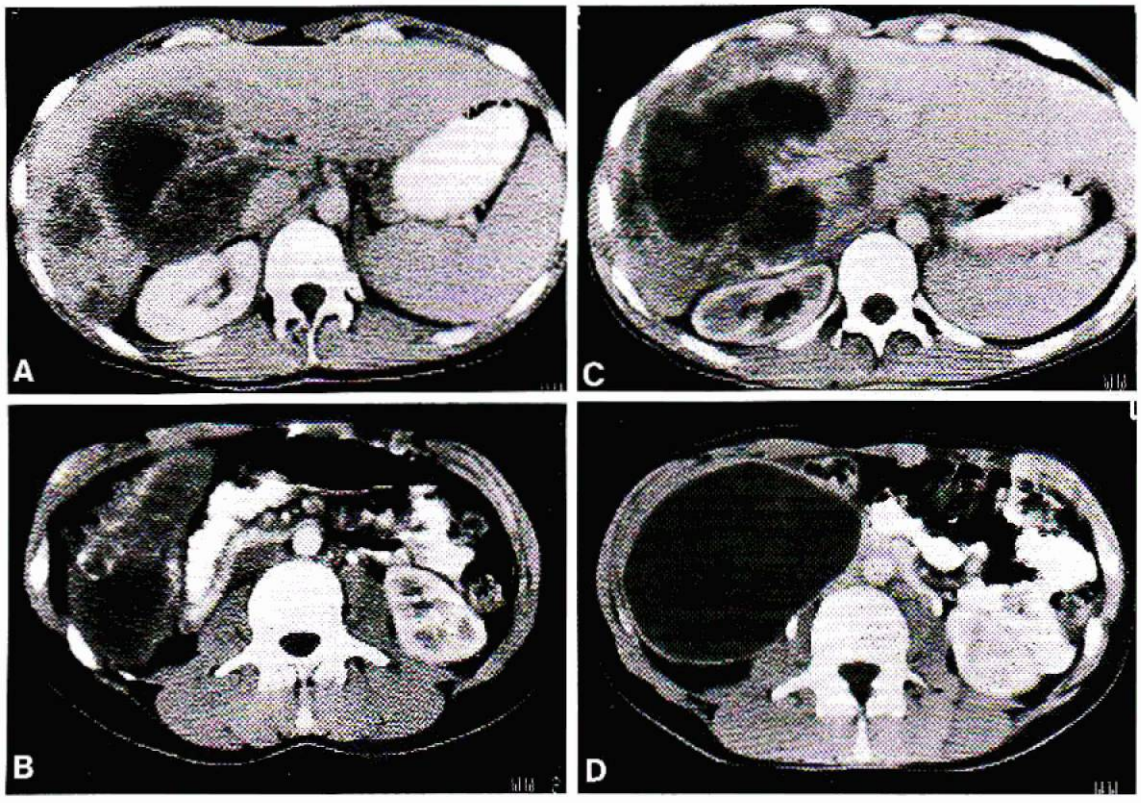

Fig. 5 A, B. Mass in midportion of right lobe. *1983:* **A section at the level of the hepatic hilum; B section at the level of L4.** *1988:* **C, D** comparable sections showing a significant increase **in the size of the mass, mainly due to massive necrosis predominating in the inferior portion.** Presence of intralesional gas (enteric fistula?)

if necrotic; in 1 case of regression of a necrotic lesion, there was development of portal hypertension due to fibrotic scarring and stenosis of the portal bifurcation.

C. True evolutionary forms are relatively rare and only represent 20% of our cases with the parasitic increase. The analysis of these observations confirms the characteristically slow evolution with a long doubling time (average = 37 months); documents 2 components of the evolutionary events:

- an increase in the size which seems to occur by continuous peripheral growth or by increase of the central necrosis; preferential hilar extension [12] occurs but not common as is shown by the uncommon biliary involvement in our series;
- changes in the appearance of the lesions, related to ischemia and occurring intermittently. Within an initially homogeneous site of infection (where parasitic elements and significant fibro-inflammatory reaction are closely mixed), one sees the development of calcifications, usually distributed as microcalcifications in a peripheral fashion, then necrosis which usually occurs later with central confluent regions.

The various morphologic types described (10-11) are various evolutionary stages of a given site of infection. A given site of infection can change its evolutionary mode over time, i.e. it may progress after a few years of quiescence or stabilize after an exacerbation.

The analysis of the CT features. It allows assessment of their possible prognostic contributions

A. *Size.* Prognosis of small lesions (<4 cm) generally seems to be rather favourable, for they represent the majority of stable and regressive forms. On the other hand, a large lesion size does not constitute an unfavourable prognostic feature, as lesions greater than 15 cm in diameter have remained stable for 5 years.

B. *Calcifications,* especially microcalcifications, have no value in prognosis: they can appear while the lesion is evolving and simply represent increased ischemia within the lesion. Extensive macrocalcification seems to be associated with a favourable prognosis, especially if signs of regression are present.

C. *Necrosis* also has no value in prognosis: found in regressive forms, it can also be at the origin of a rapid increase in the size of a lesion.

Our study does not show reliable correlation between clinical or biological parameters and CT results

Clinical signs reported by patients are often minor with poorly defined pains. These clinical signs are found in stable as well as in progressive forms. Clinical and biological jaundice is not a definite sign of seriousness: always variable,

regressive, and sometimes absent for several years, it is only found in 20% of our patients. In this series, we have no documented cases of obstructive jaundice or portal hypertension; these major complications are rare, for US and CT examinations allow diagnosis at an earlier stage of the disease [3].

Because of the lack of clinical biological correlation in progressive forms, periodic CT follow-up is necessary: if the clinical state is normal, a yearly or 18 month follow-up seems to be sufficient because of the slow doubling time. If clinical or biological signs, or CT evolution, occur, the follow-up must be every 6 months. Lesion evolution, seen over several CT examinations in spite of medical treatment, must lead to contemplation of surgical intervention for palliative or curative purposes (resection or transplant).

The impact of medical treatment with Imidazole in lesion evolution remains under consideration

This treatment has been well evaluated in in vitro experiments and seems promising in human hydatid infection [3, 13]. It may be responsible for the overall lesion stability seen in our series; however, the slow and unpredictable evolutionary nature has been noted prior to the establishment of this type of treatment. In the two regressive forms in our series, one occurred prior to the establishment of medical treatment, and three of the four patients who presented with an exacerbation were treated with Imidazole therapy. Nevertheless, in some symptomatic patients, a biological or clinical improvement was noted when the treatment was established, and progression occurred when the treatment was stopped. The treatment seems more effective in extrahepatic locations [14, 15]. Because of these positive features in addition to its very low toxicity, treatment should be continued, but patients should also continue to undergo regular CT follow-up.

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