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FRENCH ASL CASES

With my letter of 1 November 1978 I gave some of you a photocopy of a paper by the French Works Medical Officers of the ten ASL cases so far encountered in France. I said that when things were a bit quieter I would do some rough translation. Now the French are up to eleven ASL cases I thought I had better get on with it. I do apologise, it is a very rough translation and probably medically inexact. I did not translate the tables which I think will be quite clear to all of you.

John Stafford

Encs

R&S 106054

TEN CASES OF LIVER ANGIOSARCOMA

EXPERIENCED IN WORKERS EXPOSED TO VCM

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PAPER PRESENTED TO THE 19TH INTERNATIONAL OCCUPATIONAL MEDICINE CONFERENCE AT DUBROVNIK ON 28 SEPTEMBER 1978 BY :

DRS J BERROD - P LAZARD - C PIERRE - A M PUECH - E RAVIER - J RETY - G SMAGGHE -

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At the end of the Viola and Maltoni experiments the publication of the evidence of the carcinogenic action of VCM and particularly the induction of ASL by this chemical agent led, as one might expect, to a large number of studies, particularly experimental studies.

The Works Medical Doctors found themselves, however, confronted in their factory activities by practical problems of surveillance and prevention.

It seemed likely that a worker newly recruited into the factories would be exposed only to a very small risk as a result of the effective technical measure taken during the past few years. But a considerable number of workers still employed in the factory or retired had been exposed for a number of years to concentrations of VCM which in former times seemed harmless but which in the light of recent information seemed possible agents for the induction of angiosarcomas.

Knowing the evolution of this disease, it can seem fruitless to interest oneself in finding means of early detection of ASL.

Nevertheless, we have been able to observe the case of a patient having undergone a surgical intervention with a survival of about two years, although the diagnosis had only been taken to the stage of clinically detectable lesions.

Without ignoring the many fold and well known difficulties of cancer therapy, we consider that it is not useless to try to discover as early as possible an ASL lesion and allow the different skilled specialists to give an efficient therapy.

With this in mind we have applied ourselves to the detailed study of the ten cases of ASL diagnosed in France in workers exposed to VCM.

It is not possible for us, of course, in the time available to look in detail at the observations which consist of the precise data on previous occupation, clinical history, the results of various practical examinations, therapies, the results of anatomo-pathological examinations, etc. We can communicate these data to anyone in the audience interested if they should wish.

We have assembled in the tables the principal elements in our observations to try to display the relevant data leading up to our surmise of a diagnosis.

We hope that these tables will be sufficiently legible and we will comment on them briefly.

Table No 1

Table No 1 shows that the ten cases studied were all exposed for a long time at high concentrations (11 years minimum and most of the time cleaners of autoclaves or polymerisation workers) the youngest case being 38 yrs and the oldest case 62 yrs : in processes of making emulsion, suspension and mass PVC).

It should be noted that case no 1 was diagnosed in 1967 and that he was found again as a result of an epid miological study conducted in our factories. Th diagnosis has been confirm d histo-pathologically in the t n cases

Table No 2

In Table No 2 we have gathered together previous history and tried to enumerate clinical symptoms from the first appearance.

We would point out in this comparison one case only (No 4) with a record of alcohol intake and consequent hepatic troubles(?), one case (No 7) with an indisputable acro-osteolysis one year before the discovery of the ASL, one case (No 9) which presented itself after biological tests 4 years previously had shown a transitory increase of alkaline phosphatase and jaundice. Finally, in Case No 5 it was the fortuitous discovery of an angiosarcomatose costal tumour which led the works doctor to ask a specialist to look systematically for an ASL.

This table displays the poverty of clinical signs of the initiation of trouble, the initial symptoms often being either an acute or haemorrhagic phenomenon or a rapid loss of weight accompanied by debility.

In the majority of cases at the time of diagnosis the liver appears augmented in volume (8 times out of 10) and the spleen was also clinically enlarged (7 cases out of 10).

Table No 3

Table No 3 lists the complementary practical examinations, eg scintigraphy laparoscopy and arteriography. In most cases the appearance of abnormal pictures of the right lobe and the good reproducability of these examinations which are in a good state of practical evolution reinforces clinical suspicions which are already strong.

Table No 4

Table No 4 indicates to us that in a number of cases the haemorrhagic symptoms are a characteristic of the evolution of the disease (6 out of 10). Th treatment has been surgical in all the cases.

In one case there was an exploratory laparotomy; in the other cases a s gmentary hepatectomy, a multi segmentary hepatectomy or right lobe. A tw nty month survival in Case No 9 is to be noted.

Furthermore one must note that Case No 7 survived thirteen months aft r the removal of a hemat misis(?) resulting from a local haemorrage near th angiosarcoma.

Radiotherapy was used in association with surgical treatment in one cas only (No 8). In Case No 5 radiotherapy was done locally near the bony lesion.

Table No 5

Table No 5 gives the histopathological data. One must note the spongy aspect of the lesions in five cases, sinusoidal in four cases, papillary in two cases and massive in two cases.

Th non-cancerous fibrosis of the parenchyma is weak in five cases, much mor marked in one case (No 4). The xtent of the lesion is in general very local (Nos 1,3,6, 7 and 8) it is bony (costal) in Case No 5 which is th only case in our obs rvations wh r on has had any vidence of metastasis.

Table No 7

Table No 7 is confined to Case No 10. This case was found diagnostically at the beginning of this year. His medical dossier comprises a series of examinations which we have displayed.

It is notable that the alkaline phosphatase is raised (10.4 units against a normal of 3 units) and a bilirubin of 12 mg/litre (N 10 mg) only one month after hospitalisation with normal transaminases and normal alpha-foeto protein (6.5 - N 15). The alkaline phosphatase stayed high on 3 January 1978 (one month afterwards) the transaminases were always normal and stayed so three days before surgical intervention. They only seemed high (157 and 113 units against a normal 40) on the day of the surgical operation.

Anaemia with 3.4m hematocytes appeared only on the 7th January with a normal number of thrombocytes (day of operation).

At this time arteriography had already shown an irregularity on the right lobe and scintigraphy had shown three very sharp lacunae. The slides which we will now show you show the extent of the lesions in some sections from the operation.

This example highlights the difficulty if not the impossibility of early diagnosis solely by biological investigations and the study of the ten cases has served to reinforce this impression.

Scintigraphy, arteriography, laparoscopy, even laparotomy are certainly more precise techniques, but in the range of our diagnostic tools can only be the exceptional method of investigation and not without risk.

That is why we are now turning our studies towards ultrasonography.

This test, which has the merit of being well accepted by the patients, does not carry any additional risks and seems to be capable as the technique progresses to disclose abnormal pictures with good resolution in the liver parenchyma, and seems to us capable of giving valuable information to a early diagnosis and in conjunction with biological examinations limits the number of patients who must be exposed to diagnostic techniques which are more invasive and risky.

J Stafford

JS/MJE/DSO-107
2 February 1979

Tableau I

CAS	DATE DE NAISSANCE	EXPOSITION AU C.V.M. DE	A	ANNEES 1ère EXPOSITION AU DIAGNOSTIC	ANNEES EXPOSITION	DEGRE EXPOSITION	DATE DU DIAGNOSTIC	DATE DU DECES	AGE ET SITUATION AU DECES	EMPLOI
N° 1	15.4.24	1946	1967	21	19	+++	19.2.67 (étude épidémio. anapath.)	19.2.67	43 (a)	Conducteur-décroûteur
N° 2	3.6.11	1959	1971	16	12	+++	1975 (anapath.)	24.1.75	63 (r)	Polymérisation
N° 3	6.1.20	1946	1975	29	29	+++	15.1.75 (anapath.)	26.6.75	55 (a)	Décroûteur (10 ans) Synthèse du CV (16 ans) Compounds (3 ans)
N° 4	27.1.27	1949	1975	26	26	+++	16.1.76 (autopsie)	3.1.76	49 (a)	Synthèse du CV (8 ans) Filtration du PCV (18 ans)
N° 5	29.1.38	1965	1976	11	11	+++	autopsie	13.5.76	38 (a)	Conducteur (10 ans) Décroûteur (1 an)
N° 6	26.4.27	1950	1972	26	22	+++	autopsie	2.7.76	49 (m)	Polymérisation (Agent de Maîtrise)
N° 7	14.4.34	1958	1971	18	13	++	12.9.76 (autopsie)	12.9.76	42 (a)	Polymérisation
N° 8	1.4.34	1957	1976	19	19	++	1.12.76 (anapath.)	30.1.77	43 (a)	Décroûteur Conducteur
N° 9	8.10.14	1948	1976	28	28	+++	26.4.76 (anapath.)	25.12.77	62 (a)	Polymérisation
N°10	24.5.19	1956	1977	21	21	+++	1.78 (anapath.)	20.1.78	58 (a)	Décroûteur Conducteur

a = activité r = retraité m = m

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Tableau II : antécédents. Symptomatologie initiale

CAS	DUREE D'EXPOSITION	ETHYLISME OU ANTECEDENTS HEPATIQUES	ANTECEDENTS	MODE DE DEBUT Symptome révélateur	AUTRES SIGNES FONCTIONNELS	SIGNES PHYSIQUES				
						FOIE	RATE	ASCITE	ICTERE	TUMEUR PALPABLE
1	19	0	Céphalées Hépatomégalie Murphy +	Hémopéritoine	-	+	-	-	-	
2	12	0	Gastrectomie (ulcus) Rectorragies	Douleur hypocondre droit Anémie	-	+	+	+	-	
3	29	0	Ulcère duodénal ~~3 ans avant~~	Masse douloureuse épigastrique	Amaigrissement 12 Kg en 6 mois	+	-	-	-	+
4	26	++	-	↓ Etat général Douleur hypocondre droit à un examen systématique	-	+	-	+	+	
5	11	-	Accident de trav. Bil. 12 à 18mg/l un an avant	Angiosarcome osseux	-	-	-	-	-	
6	12	0	Fibrillation ventriculaire	Tableau de cholécystite	Amaigrissement Anorexie. Asthénie T° à 38°	+	-	-	Subictère au début	
7	13	-	Acro-ostéolyse melocnas 1 an avant	Syndrôme douloureux pseudo perforatif	Défense épigastrique. T° à 37°8	-	-	-		
8	19	-	Valvulite mitro aortique	Nausées post prandiales	-	+	+	-	-	
9	28	-	Contusion hypochondre drt. subictère ↑ PA 4 ans avant	Douleur hypochondre droit	Amaigrissement T° à 37°5-38°	+	-	-	-	-
10	28	0	Cure de hernie inguinale g. HTA (1976) Taenias	Asthénie	Amaigrissement 3 Kg en 3 sem. Pesanteur épigastrique.	+	+	0	0	Hépatomégalie régulière.

- SCINTIGRAPHIE - - LAPAROSCOPIE - - ARTERIOGRAPHIE -

CAS N°	FOIE		FIXATION SPLENIQUE	MASSE TUMORALE	HEPATO MEGALIE	HTP	RATE	SYNDROME TUMORAL LOCALISATION	HYPER VASCULARISATION	GENE AU RETOUR VEINEUX	ARTERE HEPATIQUE	DILATATION ARTERE SPLENIQUE	RATE
	Aspect	Localisation											
1	Malade décédé avant tout examen complémentaire												
2	Lacunes multiples	Lobe droit	+	Foie masqué par des adhérences				+ Lobe droit			Issue de l'AMS	+	+
3	2 lacunes	Lobe droit		Non faite				+ Lobe droit	+	+	D=N C=Grêle	+	
4		Non faite		+	+	+	+	+ diffus	+	+	dilatée		+
5	1 lacune	Lobe droit	+	+	-	-	-	+ Lobe droit		+		+	+
6	1 lacune	Lobe droit		+ (masse)	+	-	-	+ Lobe droit	+				
7		Non faite		Non faite				+ Lobe droit	+			+	+
8	Hétérogène	Diffus	+	+	+			+	+				
9	2 lacunes	Lobe droit		Pas de données				+ Lobe droit	+				
10	3 lacunes	Lobe droit		+	+	-	+	Lobe droit	0				+

Tableau III : examens complémentaires

Tableau IV : évolution

CAS	EVOLUTION	TRAITEMENT			SURVIE	DECES
		Chirurgie	Chimiothérapie	Radiothérapie		
1		Hépatectomie droite			1 jour	post-opératoire
2	Hémopéritoine	Hépatectomie droite Splénectomie			3 mois	Hémorragies digestives Coma hépatique
3	Meloenas	1) Exérèse tumeur 2) Résection duodénale et antrectomie	+		6 mois	Coma hépatique
4	Hématémèse Syndrôme oedémato ascitique	Hépatectomie droite Splénectomie Cholécystectomie	+		3 mois	Hémorragies digestives
5	Hémopéritoine	Hépatectomie droite Splénectomie Cholécystectomie	+	+ pour tumeur osseuse	8 mois	Choc Hémorragies internes
6	Etat général Masse droite Septicémie	Hépatectomie segmentaire			6 mois	Coma hépatique Septicémie
7	Etat général Amaigrissement Douleurs abdominales violentes Hémorragies digestives	Evacuation hématome			13 mois	Hémorragies digestives Fistulisation à la peau
8	Ascite-Hémorragies (rectorragies) Dénutrition	Laparotomie exploratrice		+ (1 000 rads)	3 mois	Hémorragie digestive
9	Fistule biliaire à la peau puis fistule bilio-bronchique	Hépatectomie pluri-segmentaire			20 mois	Post-opératoire après fistule bilio-bronchique opérée 20 mois après la 1ère intervention.
10	Embolie pulmonaire	Hépatectomie droite Cholécystectomie Surrénalectomie droite			10 jours	Embolie pulmonaire

Tableau V : Anatomo-pathologie

CAS N°	FOIE Poids	TUMEUR (formes)				PARENCHYME NON TUMORAL				RATE	EXTENSION	B.CHIRURGICALE	AUTOPSIE
		Ginusoïdale	Papillaire	Caverneuses	Massives	Epaississement capsulaire	Fibrose	Dilatation sinusoïdes	Cellules endothéliales atypiques			diagnostic positif ++	
1											Veine cave		++
2	1610g	+		+	+		+		+	HTP 460g	0	++	+
3		+		+	+		+		+		Duodénum	++	+
4	2230g	+	+	+			++	+	+	HTP 400g	0		++
5	600 g lobe droit					+	+	+	+	HTP 650g	Osseuse surrénale gauche	++	+
6				+		+	+ peu importante		+		Grêle	+	++
7	1750g		+	+			+	Peliose +		HTP	Diaphragme colon paroi abdominale	+	++
8	3000g	données insuffisantes								270g	Ganglions aortiques	++	+
9	950g	+			+		-	+				++	
10	1560g (pièce exérèse)		+		+	+	+	+	+			++	++

Tableau VI : Surveillance hématologique CAS N° 10 (de 1974à1978)

DATES	GR	Hgb	VGM	LEUCO	PN	EO	BASO	LYMPHO	MONO	MYELO	META MYELO	THROMBO CYTES	VS 1 H
21.11.74	4,2	13,4	93	5 300	24	6	0	44	12	2	12	215 000	6
19.1.76	4,54	14,4	99	5 700	54	1	0	34	11	-	-	160 000	2
26.10.76	4,36	13.8	94	6 700	48	3	0	39	10	-	-	220 000	3
1.12.77	4,24	13,5	-	10600	51	2	0	34	13	-	-	-	-
7.1.78 (3 jours avant intervention)	3,6	10,3	-	10900	-	-	-	-	-	-	-	-	-

Tableau VII : Surveillance Biologique CAS N° 10 (de 1974 à 1978)

DATES	TOTALE BILIRUBINE mg/l	P.A.	S.G.O.T	S.G.P.T.	ELECTRO-PHORESE PROTEINES	LDH	GT	OCT	FOETO PROTEINES
21.11.74	7	-	28 N 19	16 N 19	Normale	-	-	-	-
19.1.76	7	66 N 85	10 N 19	7 N 19	-	-	-	-	-
26.10.76	6	6 N 85	8 N 19	6 N 19	-	162 N : 96/240	15 N 28	11 N 10	-
1.12.77	12	10,4 UB N 3	29 N 40	34 N 40	CONSULTATION pour symptomatologie de début apparent		-	-	6,5 mg N 15
3.1.78	4	11,2 UB N 3	17 N 40	21 N 40	-	-	-	-	-
7.1.78	-	-	21 N 40	23 N 40	NB : 3 jours avant intervention chirurgicale				
10.1.78	-	-	157 N 40	113 N 40	NB : jour de l'intervention chirurgicale				