DIAGNOSTIC HISTOPATHOLOGIQUE

Le diagnostic histopathologique du mésothéliome constitue une étape essentielle de la prise en charge des patients, à la fois dans l'optique de la prise en charge thérapeutique et dans celle de la reconnaissance d'une maladie professionnelle (6,7). Il s'agit d'un diagnostic difficile, devant faire appel à des pathologistes expérimentés ; l'examen extemporané est de ce fait prohibé. Le diagnostic cytologique est en règle insuffisant ; des prélèvements biopsiques de taille suffisante, habituellement effectués par thoracoscopie, voire thoracotomie, sont indispensables pour effectuer le diagnostic qui requiert une confirmation immunohistochimique. Chez les patients fragilisés, une biopsie transcutanée sous contrôle tomodensitométrique, éventuellement précédée d'une tomographie à émission de positons, peut parfois s'avérer suffisante.
La morphologie des mésothéliomes pleuraux malins est variable, avec environ 70% de formes épithélioïdes, 10% de formes biphasiques ou mixtes et 15% de formes fusiformes ou sarcomatoïdes selon l'OMS 2015 (8,9)
La démarche diagnostique passe par deux étapes : la première étape est d'affirmer la malignité de la lésion ; il est parfois difficile de différencier une hyperplasie mésothéliale atypique d'un mésothéliome malin épithélioïde débutant ou de voisinage, ou une pachypleurite d'un mésothéliome desmoplastique. La mise en évidence d'une délétion homozygote du gène *CDKN2A* (p16) par FISH constitue un argument important en faveur d'un mésothéliome dans les cas difficiles. De même, la perte d'expression de BAP1 en immunohistochimie apparaît très spécifique pour affirmer le diagnostic de mésothéliome malin en cas de doute diagnostique avec une hyperplasie mésothéliale atypique (10). La mise en évidence sur prélèvement cytologique (cytobloc) d'une prolifération mésothéliale avec délétion homozygote du gène *CDKN2A* et/ou perte d'expression de la protéine BAP1 doit faire privilégier l'hypothèse d'un mésothéliome malin, qui ne peut être affirmé sur la morphologie seule. La seconde étape consiste à différencier le mésothéliome malin d'une autre prolifération tumorale pleurale. Les formes mixtes posent le problème du diagnostic différentiel avec le synovialo-sarcome et les formes sarcomatoïdes avec un sarcome ou un carcinome sarcomatoïde, mais le problème le plus fréquent est celui de la distinction entre métastase pleurale d'un adénocarcinome et mésothéliome pleural malin. L'immunohistochimie est alors primordiale (cf tableau 1).

A savoir que les mésothéliomes sarcomatoïdes sont parfois uniquement positifs pour les cytokératines, plus rarement pour la calrétinine ; il faut éliminer un sarcome (le mésothéliome peut être desmine et actine positif) ou une tumeur solitaire fibreuse de la plèvre (le mesothéliome est CD34 et STAT6 négatif) ou encore une métastase d'un carcinome sarcomatoïde (qui peut être TTF1 ou P40 positif).
Les échantillons doivent être adressés au panel d'anatomopathologistes spécialisés (groupe NETMESO/MESOPATH (11)), sans que cela ne retarde la décision thérapeutique ou légale.

Recommandations

-Le diagnostic histologique du mésothéliome pleural malin doit être effectué sur des prélèvements biopsiques de taille suffisante (thoracoscopie sauf contre-indications). L'examen extemporané n'est pas accepté pour ce diagnostic.
-Le diagnostic morphologique doit toujours être complété par une étude immunohistochimique confirmative.
-Le diagnostic histopathologique doit être confirmé par l'expertise du réseau NETMESO/MESOPATH après transmission à un expert régional du réseau, dans l'optique d'une indemnisation par le FIVA et/ou la CPAM.

Critères	Mésothéliome	Adénocarcinome
	Histochimie	
	Absence de vacuoles cytoplasmiques de mucus	Vacuoles de mucus cytoplasmiques (PAS + diastase) parfois
	Immunohistochimie	
Cytokératines (AE1-AE2, KL1, CK8-18, ..)	+	+
EMA	souvent + membranaire	souvent + cytoplasmique diffus
ACE	-	souvent +
Ber EP 4	- (20% +)	souvent + (60%)
Calrétinine*	+	-
Cytokératine 5/6	+	-
WT1	+ nucléaire	-
Récepteur oestrogènes	-	Parfois +
TTF1	-	souvent +

Tableau 1 – Aspect histochimique et immuno-histochimique comparé du mésothéliome épithélioïde et de l'adénocarcinome

** Marquage nucléaire et cytoplasmique. Seul le marquage nucléaire est spécifique du mésothéliome. Un minimum de deux marqueurs pour le mésothéliome positifs ET deux marqueurs pour l'adénocarcinome négatifs sont requis pour le diagnostic.*

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