



eBreast Práctica Cáncer de Mama

**MANUAL PRÁCTICO PARA LA CONSULTA
DE PACIENTES CON CÁNCER DE MAMA**

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Avales

PARA INFORMACIÓN ADICIONAL, CONSULTAR EL RESTO DE LOS CAPÍTULOS

PRÓLOGO

eBreast nace como signo de los tiempos.

No es un libro.

No es una app.

Es la respuesta a las nuevas formas de aprender, enseñar y estudiar.

Signo de los tiempos por la importancia y el impacto que tiene el cáncer de mama en nuestra sociedad y en nuestro sistema sanitario.

Signo de los tiempos por la incesante llegada de nuevos profesionales que tienen la gran responsabilidad de cuidar a nuestras pacientes afectas de cáncer de mama y con la necesidad de adquirir un conocimiento riguroso, actualizado y de acceso inmediato, a veces en la propia consulta, para poder ofrecer las mejores opciones que la evidencia científica nos proporciona.

Signo de los tiempos por la forma de enfrentarse a la información. La aparición y expansión de nuevas TIC (Tecnologías de la información y comunicación), algunas de ellas rápidamente absorbidas por las nuevas generaciones, hace preciso adaptarse a ellas.

Signo de los tiempos por el enorme volumen de información que se genera a diario y que hace precisa la intervención de revisores autorizados en cada materia, sobre todo para los clínicos. El fondo de conocimiento médico es inabarcable. Y el conocimiento y el progreso oncológicos son, actualmente, de los más importantes en la medicina moderna: por volumen de publicaciones, recursos que se destinan, impacto social, consecuencias de la enfermedad...

eBreast está dirigido a todos aquellos profesionales que atienden una consulta médica de cáncer de mama, sobre todo a los que se inician en la patología, a los que atienden a estas pacientes de forma más esporádica o simplemente a los que desean mantenerse actualizados. eBreast proporciona una consulta rápida, sencilla y, sobre todo, muy visual e interactiva. Y con este proyecto nos comprometemos a revisar periódicamente los contenidos, actualizando los datos tras los principales acontecimientos científicos del año.

Los coordinadores quisiéramos agradecer el inmenso esfuerzo realizado por todos los autores, así como el apoyo proporcionado por Novartis, y a las sociedades GEICAM, SEOM, SOLTI y a la Universidad CEU Cardenal Herrera por su aval.

No queremos dejar de olvidar el apoyo de nuestras familias y, sobre todo, a LOS/LAS PACIENTES afectos de cáncer de mama, que son el objeto de todos nuestros esfuerzos, estudios y desvelos profesionales y por tanto, los beneficiarios finales de este proyecto, que pretende ser novedoso.

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ABREVIATURAS

A	Antraciclina
AC	Adriamicina/doxorrubina, ciclofosfamida
ACT	Antraciclina-ciclofosfamida y taxano concurrente
AC-T	Antraciclina-ciclofosfamida y taxano secuencial
AC-D	Adriamicina, ciclofosfamida, docetaxel
AL	Adriamicina Liposomal
ALND	<i>Axillary lymph node dissection</i>
AMH	Agente modulador del hueso
ANA	Anastrozol
AO	Ablación ovárica
AP	Adriamicina,paclitaxel
APBI	Radioterapia parcial acelerada
AP-CMF-Q(x)	Adriamicina y paclitaxel-quimioterapia de ciclofosfamida, metotrexato y 5-FU
AP-CMF	Adriamicina y paclitaxel, ciclofosfamida, metotrexato y 5-FU
ASCO	<i>Sociedad Americana de Clínica Oncología</i>
AxRT:	<i>Axillary radiotherapy</i>
B	Bevacizumab
BAG	Biopsia con aguja gruesa
BAV	Biopsia asistida por vacío
BC	Beneficio clínico
BCS	Supervivencia específica por cáncer de mama
BOADICEA	<i>Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm</i>
BSGC	Biopsia selectiva del ganglio centinela
CAF/FAC	Ciclofosfamida, adriamicina y 5-FU
CAFM	Ciclofosfamida, adriamicina, 5-FU y metroxetato
C	Cirugía/Carboplatino
CAP	Capecitabina
CC	Cirugía conservadora
CDDP	Cisplatino
CDI	Carcinoma ductal invasivo

CDIS	Carcinoma ductal <i>in situ</i>
CDK	Cinasas dependientes de ciclinas
CEA	Antígeno carcinoembrionario
CEF/FEC	Ciclofosfamida, epirrubicina, 5-FU
CLI	Carcinoma lobulillar infiltrante
CM	Cáncer de mama
CMAJ	<i>Canadian Medical Association Journal</i>
CMF	Ciclofosfamida, metotrexato y 5-FU
CMI	Cáncer de mama inflamatorio
CMLA	Cáncer de mama localmente avanzado
CMM	Cáncer de mama metastásico
CMTN	Cáncer de mama triple negativo
cN+	Ganglios linfáticos positivos clínicamente
C-A-CMF	Cirugía-antraciclina-ciclofosfamida, metotrexato y 5-FU
C-AP-CMF	Cirugía-adriamicina, paclitaxel-ciclofosfamida, metotrexato y 5-FU
D	Docetaxel
ddAC	Dosis densas adriamicina y ciclofosfamida
DMO	Densidad mineral ósea
DX	Doxorrubicina
EBCTCG	<i>Early Breast Cancer Trialists' Collaborative Group</i>
EC	Epirrubicina, ciclofosfamida
ECG	Electrocardiograma
ECO	Ecografía
ED	Epirrubicina, docetaxel
ESA	Agente estimulador de la eritropoyesis
ESMO	European Society for Medical Oncology
EXE	Exemestano
F	Fulvestrant
FEVI	Fracción de eyección ventricular izquierda
FN	Fiebre neutropénica
GC	Ganglio centinela
GnRH	Hormona liberadora de gonadotropina

G-CSF	Factor estimulante de colonias de granulocitos
TR	Trastuzumab
HD	Altas dosis
HER/EGFR	Receptor de factor de crecimiento epidérmico humano
HNA	Hormonoterapia neoadyuvante
HR	<i>Hazard ratio</i>
HT	Hormonoterapia
IA	Inhibidores aromatasa
IAE	Inhibidor no esteroideo de la aromatasa
IANE	Inhibidor de la no esteroideo de la aromatasa
IC	Intervalo de confianza
ICT	Células tumorales aisladas
IHQ	Inmunohistoquímico
ILE	Intervalo libre de enfermedad
IPM	Irradiación parcial de la mama
ISH	Hibridación <i>in situ</i>
L	Lapatinib
LA	Linfadenectomía axilar
LET	Letrozol
LHRH	Hormona liberadora de la hormona luteinizante
LR-SLP	Supervivencia libre de progresión locorregional
MMSE	<i>Mini-Mental State Examination</i>
MNA	<i>Mini nutritional assessment</i>
MRM	Mastectomía radical modificada
MT	Marcadores tumorales
N.A	No aportado
NAB-P	nab-paclitaxel (paclitaxel unido a albúmina)
NCCN	<i>National Comprehensive Cancer Network</i>
NCI	<i>National Cancer Institute</i>
NCI-CTCAE	<i>National Cancer Institute Common Terminology Criteria for Adverse Events</i>
N.S	No significativo
NSABP	<i>National Surgical Adjuvant Breast and Bowel Project</i>

OCCR	<i>Ovarian Cancer Cluster Region</i>
OR	<i>Odds Ratio</i>
ORR	<i>Objective response rate</i>
OSNA	<i>One step nucleic acid amplification</i>
P	Paclitaxel
PA	Palbociclib
PAAF	Punción aspiración con aguja fina
PE	Progresión de la enfermedad/pertuzumab
PEPI	<i>Preoperative Endocrine Prognostic Index</i>
PER	Pertuzumab
PET	Tomografía por emisión de positrones
PF	Preservación de la fertilidad
Post-Op	Postoperatorio
PP	Profilaxis primaria
pRC	Respuesta patológica completa
Pre-Op	Preoperatorio
pRP	Respuesta parcial patológica
pRPmic	Respuesta parcial patológica microscópica
PS	Profilaxis secundaria
QoL	Calidad de vida
QT	Quimioterapia
RANKL	Ligando del receptor activador del factor nuclear k-B
RC	Respuesta completa
RCB	<i>Residual Cancer Burden</i> (enfermedad residual posquimioterapia)
RE	Receptor de estrógeno
RFS	Supervivencia libre de recaída
RH	Receptor hormonal
RMN	Resonancia magnética nuclear
ROI	Rastreo óseo isotópico/ gamma o escintigrafía ósea
RP	Receptor de progesterona/Respuesta parcial
RR	Riesgo de recaída
RS	Recurrence score

RT	Radioterapia
Rx	Radiografía
SBRT	Radioterapia estereotáctica de cuerpo
SC	Subcutáneo
SERD	Inhibidor selectivo del RE
SERMS	Modulador selectivo del receptor estrogénico
SG	Supervivencia global
SLE	Supervivencia libre de enfermedad
SLP	Supervivencia libre de progresión
SLR	Supervivencia libre de recaída
SNP	<i>Single nucleotide polymorphism</i>
SPPB	Batería corta de rendimiento físico
ST	Tratamiento sistémico
T	Taxano
TA	Tratamiento adyuvante
TAC	Tomografía axial computarizada o Docetaxel, adriamicina, ciclofosfamida
TAM	Tamoxifeno
TBCRC	<i>Translational Breast Cancer Research Consortium</i>
TC	Docetaxel y ciclofosfamida
TCH	Docetaxel, carboplatino, trastuzumab
T-DM1	Trastuzumab emtansina
TE	Terapia endocrina
TIL	<i>Tumor Infiltrating Lymphocytes</i>
THP	Tiempo hasta progresión
TMA	Transplante de células madre autólogo
TN	Triple negativo
TNA	Tratamiento neoadyuvante
TR	Trastuzumab
UCGC	Unidad de consejo genético en cáncer
UI	Unidades Internacionales
V	Vinorelbina

CAPÍTULO 7. SITUACIONES ESPECIALES

A. CÁNCER DE MAMA EN EL VARÓN

¿Cuál es su incidencia y factores de riesgo?

¿Cuál es su tratamiento?

VER RESUMEN

7. Situaciones especiales
a) Cáncer de mama en el varón



¿Cuál es su incidencia y factores de riesgo?

INCIDENCIA Y FACTORES DE RIESGO

El cáncer de mama masculino es raro, suponiendo menos del 1 % de todos los carcinomas de mama (508). La edad media al diagnóstico es entre 60 y 70 años, aunque puede aparecer a cualquier edad.

Son factores de riesgo de cáncer de mama en el varón:

- La exposición a la radiación.
- La administración de estrógenos y enfermedades asociadas a hiperestrogenismo, como la cirrosis o el síndrome de Klinefelter.
- Las familias portadoras de mutaciones de BRCA2 en el cromosoma 13q tienen un mayor riesgo de cáncer de mama en el varón.

En el caso del varón, la aparición de una tumoración mamaria suele ser el motivo de la consulta. Las exploraciones complementarias son las habituales para el diagnóstico del **cáncer de mama** (historia clínica, exploración física, ecografía, mamografía, biopsia para determinación de RH y HER2).

La supervivencia de los hombres con cáncer de mama es similar a la de las mujeres con tumores del mismo estadio y características, aunque el cáncer de mama en el varón suele presentarse en estadios más avanzados, lo que puede empeorar su pronóstico.



Histopatología

Aproximadamente un 80-90 % de los cánceres de mama en los hombres tienen receptores de estrógenos positivos y el 65-92 % de receptores de progesterona positivos (509, 510).

En definitiva, aunque en el enfoque diagnóstico y terapéutico del cáncer de mama del varón se extrapolan muchos resultados del cáncer de mama en la mujer, algunos grupos han hecho un gran esfuerzo en el registro retrospectivo de los casos en el varón. Es el caso de los datos descritos por Cardoso y colaboradores del estudio EORTC 10085/TBCRC/BIG/NABG, en el que se evaluaron los factores anatomopatológicos pronósticos; se realizó una revisión anatomopatológica central de 1.203 casos, de los 1.483 pacientes con cáncer de mama en el varón tratados entre 1990 y 2010 en 93 centros de nueve países. De los 1822 pacientes incluidos, se analizaron 1483, el 63.5% habían sido diagnosticados entre el 2001 y el 2020. La mediana de edad fue de 68.4 años. Un 5.1% presentaban enfermedad metastásica, Entre los pacientes sin afectación metastásica, el 56.2% no tenían afectación ganglionar, y el 48% tenían tumores T1. En un 4% se realizó cirugía conservadora, en un 18% se realizó biopsia del ganglio centinela. Un 29.8% realizó quimioterapia adyuvante, y un 76.8% tratamiento hormonal, principalmente tamoxifeno (88.4%). La revisión anatomopatológica central confirmó que en un 84.8% se trataba de carcinomas ductales infiltrantes, en un 51.5% de grado 2, con positividad para receptores de estrógenos en un 99.3%, de progesterona en un 81.9%, y de andrógenos en un 96.9%. Utilizando parámetros inmunohistoquímicos, un 41.9% podían ser clasificados como luminal A, un 48.6% como luminal B HER2 negativo, un 8.7% presentaban positividad para HER2, y solo un 0.3% se clasificaron como triple negativos. La expresión de receptores de estrógenos, progesterona y andrógenos se asoció significativamente a mejor supervivencia global y supervivencia libre de recidiva. Sin embargo, no se encontró asociación entre supervivencia global o supervivencia libre de recidiva y estado de HER2, Ki 67 o subtipos determinados por inmunohistoquímica. Se apreció un incremento significativo de supervivencia a lo largo del tiempo (511).

En otra revisión de 97 pacientes, el cáncer de mama en el varón se asoció a mayor positividad de RH y a menor sobreexpresión de HER2 que el cáncer de mama en la mujer; presentando proporciones similares a las de la mencionada serie de Cardoso. En esta serie, sin embargo, el grado histológico 3 y el ki-67 > 20 % se asociaron a una peor supervivencia (512).



¿Cuál es su tratamiento?

TRATAMIENTO

El enfoque terapéutico del cáncer de mama en el varón no difiere del tratamiento general del cáncer de mama.

Cirugía

- **Mamaria:** La cirugía más común en los hombres es la mastectomía radical modificada. No es habitual que se realice una cirugía conservadora, debido al pequeño tamaño de las mamas de los hombres.
- **Axilar:** Al margen del vaciamiento ganglionar axilar, en caso de ausencia clínica y ecográfica de adenopatías axilares, la práctica de la biopsia del ganglio centinela es posible. Aunque existe menor evidencia, diferentes experiencias publicadas respaldan el uso de la biopsia del ganglio centinela en las mismas indicaciones que en la mujer (513, 514).

Radioterapia

Las indicaciones para radioterapia no son diferentes entre hombres y mujeres; los resultados se extrapolan de los resultados de los grandes estudios con mujeres. Existen pequeños estudios retrospectivos que han demostrado que la radioterapia posoperatoria en hombres también disminuye el porcentaje de recurrencia locorregional a los cinco años (515, 516).

Las indicaciones del manejo posoperatorio con radioterapia dependerán de factores como: tamaño tumoral, extensión a la piel, areola, músculo pectoral mayor, número de ganglios afectados y márgenes quirúrgicos positivos. Como ocurre en la mujer, la dosis estándar de radioterapia es de 50 Gy en 25 fracciones; los campos de radioterapia son similares a los que se aplican a la mujer.

Hormonoterapia

Indicada en caso de cáncer de mama con RH positivos.

El tamoxifeno es el tratamiento del que se dispone más evidencia, tanto en estudios en pacientes con cáncer de mama metastásico como en estudios en adyuvancia (517-520). En las tablas siguientes podemos ver algunos estudios en adyuvancia.

Tabla 84. Resultados del estudio de Ribeiro et al en adyuvancia. (517)

	N	Duración	Resultado
Ribeiro et al (517)	39	1-2 años	SLE 5a: 56 % (37-75 %)

SLE 5a: supervivencia libre de enfermedad a los cinco años

Tabla 85. Resultados del estudio de Zhou et al en adyuvancia (518)

	N	Duración	Resultado
Zhou et al (518)	32	5 años	SG 10a: 100 % para estadio I 74,2 % para estadio II 57,2 % para estadio III 50 % para estadio IV

SG 10a: supervivencia global a los 10 años

Tabla 86. Resultados del estudio de Fogh et al en adyuvancia (519)

	N	Duración	Resultado
Fogh et al (519)	42	5 años	21 recibieron TAM SG 10a: 100 % con TAM+ RT vs. 65 % TAM

SG 10a: supervivencia global a los 10 años; TAM: tamoxifeno; RT: radioterapia.

Tabla 87. Resultados del estudio de Xu et en adyuvancia (520)

	N	Duración	Resultado
Xu et al (520)	20	5 años	SG 10a: 79,6 % en el grupo adherente SG 10a: 50,4 % en el grupo de baja adherencia
	99	> 5 años	

SG 10a: supervivencia global a los 10 años

Otra alternativa son los inhibidores de la aromatasas. Algunos estudios han demostrado que los inhibidores de la aromatasas reducen los niveles de estrógenos en el varón (521). Su evidencia proviene de la descripción de algunos casos (522). El papel de estos fármacos, con o sin análogos de LHRH concurrentes, no está bien definido.

En definitiva, en el contexto adyuvante, en tumores hormonosensibles las indicaciones de la hormonoterapia (indicación, tiempo de tratamiento) procederán por analogía de los estudios de cáncer de mama en la mujer. El tamoxifeno durante cinco años será el tratamiento de elección.

En el caso de cáncer de mama metastásico, el tamoxifeno es el fármaco más extensamente utilizado en primera línea. En segunda línea de tratamiento, los análogos de LHRH, estrógenos y progestágenos pueden ser una opción. También existen casos descritos con fulvestrant (523). El papel de los inhibidores de la aromatasas, con o sin análogos de LHRH, es incierto.

Son efectos secundarios frecuentes de la hormonoterapia en el varón:

- Pérdida del deseo sexual
- Problemas de erección
- Aumento de peso
- Sofocaciones
- Cambios en el estado de ánimo

Quimioterapia y terapias biológicas

En general, los criterios y los fármacos para utilizar quimioterapia y tratamientos biológicos en el tratamiento del cáncer de mama del varón son los mismos que para el cáncer de mama en general, aunque existe poca evidencia al respecto, por la baja prevalencia de la enfermedad en varones.

Recientemente ASCO ha publicado una guía de consenso sobre el manejo del cáncer de mama en el varón, cuyas principales recomendaciones son (524):

- La mayoría de las características de manejo del cáncer de mama en el varón son similares a las usadas en la mujer.
- Los varones con cáncer de mama hormonosensible candidatos a tratamiento adyuvante deben recibir tamoxifeno con una duración inicial de 5 años. Aquellos con contraindicación a tamoxifeno, deben recibir un análogo de LHRH en combinación con un inhibidor de la aromatasa.
- En pacientes de muy alto riesgo puede ofrecerse 5 años más de tratamiento hormonal.
- Los varones afectos de cáncer de mama avanzado o metastásico hormonosensible, deben incluir tratamiento hormonal en su primera línea de tratamiento excepto en caso de crisis visceral. Los tratamientos antidiaria deben ser utilizados en enfermedad avanzada con las mismas indicaciones que las pacientes mujeres.
- La mamografía ipsilateral anual se debe ofrecer a todos los varones con historia de cáncer de mama tratados con tumorectomía, independientemente de la predisposición genética.
- La mamografía contralateral anual se debe ofrecer a los varones con historia de cáncer de mama y predisposición genética. La resonancia magnética no debe recomendarse de forma rutinaria.
- Los varones con cáncer de mama deben tener la opción de ser valorados en unidades de consejo genético y de la realización de test de los genes de predisposición.

B. TUMOR FILODES

¿Qué es y cuál es la incidencia del tumor filodes?

¿Cómo se diagnostica?

¿Cuál es su tratamiento?

VER RESUMEN

7. Situaciones especiales
b) Tumor Filodes



INCIDENCIA, PRESENTACIÓN Y DIAGNÓSTICO

¿Qué es y cuál es la incidencia del tumor filodes?

Los tumores filodes son tumores poco frecuentes (suponen menos de un 1 % de todos los cánceres de mama), compuestos tanto por elementos estromales como epiteliales (525). Se suelen dividir en subtipos benignos, *borderline* y malignos.

¿Cómo se diagnostica?

La edad de diagnóstico más frecuente es entre los 30 y los 40 años, aunque pueden presentarse a cualquier edad (526). Se presentan casi exclusivamente en mujeres, y más frecuentemente de raza blanca. Suelen presentarse en edades mayores que los fibroadenomas, pero menores que los tumores ductales y lobulillares.

El diagnóstico de estos tumores previo a la biopsia escisional o a la tumorectomía es poco frecuente, su aparición no suele asociarse a dolor. Esto se debe a que a menudo se presentan por ecografía y mamografía como fibroadenomas, e incluso la citología y la biopsia frecuentemente no permiten distinguirlos del fibroadenoma. En el contexto de una sospecha de fibroadenoma de gran tamaño y con crecimiento rápido debe sospecharse de tumor filodes. Por otra parte, el síndrome de Li- Fraumeni se asocia a un mayor riesgo de tumor filodes (527).

¿Cuál es su tratamiento?

TRATAMIENTO

Cirugía

El tratamiento principal del tumor filodes, ya sea benigno, *borderline* o maligno, es la extirpación quirúrgica con márgenes libres de ≥ 1 cm. La tumorectomía o la mastectomía parcial son los tratamientos de elección, quedando la mastectomía tan solo para los casos en los que sea imprescindible para conseguir márgenes negativos. El riesgo de recurrencia en este tipo de tumores parece marcado por la existencia de márgenes de resección libres (528).

El vaciamiento ganglionar axilar no es necesario en principio, a menos que existan ganglios afectos, ya que estos tumores raramente metastatizan a la axila (529).

Radioterapia, quimioterapia y hormonoterapia

El papel de la radioterapia complementaria es incierto. Por ello, solo se recomienda en casos de márgenes afectos sin posibilidad de que puedan ser ampliados (530).

El componente epitelial de estos tumores puede expresar receptores de estrógenos (58 %) y/ o progesterona (75 %) (531); sin embargo, la hormonoterapia no tiene evidencia demostrada en este tipo de enfermedad.

Del mismo modo, no hay pruebas de que la quimioterapia complementaria (incluyendo antraciclinas, ifosfamida, cisplatino y etopósido) proporcione un beneficio en la reducción de las recidivas o la muerte.

RECIDIVAS

Las recidivas son poco frecuentes, normalmente a nivel local, siendo la exéresis de las mismas con márgenes amplios el tratamiento de elección. Raramente existe recidiva a distancia, siendo la localización más frecuente la pulmonar; en ese caso, se recomienda administrar fármacos eficaces en el tratamiento de sarcomas de tejidos blandos.

C. CÁNCER DE MAMA Y EMBARAZO

¿Cuál es su incidencia y cómo se diagnostica? ¿Qué características presenta?

¿Cómo se trata?



¿Cuál es su incidencia y cómo se diagnostica? ¿Qué características presenta?

VER RESUMEN

7. Situaciones especiales
c) Cáncer de mama y embarazo



INCIDENCIA

El diagnóstico de cualquier cáncer durante el embarazo (durante el embarazo, el primer año de postparto o durante la lactancia) es una situación poco frecuente, con una incidencia de 1 cada 10.000 mujeres embarazadas; representa el 0.4 % de todos los diagnósticos de cáncer de mama entre los 16 y los 49 años (532). Durante el periodo gestacional las neoplasias más prevalentes son la de cervix, ovario, melanoma, hematológicas y el cáncer de mama; así, el cáncer de mama es uno de los cánceres más diagnosticados durante el embarazo, con una tendencia a incrementar debido, en parte, debido a la tendencia en posponer la maternidad (533). El diagnóstico de una neoplasia en este periodo particular de la vida de la mujer, supone un gran reto, ya que incluye la necesidad de preservar la seguridad de la gestante además de intentar asegurar la gestación, para lo que se hace imprescindible la presencia de un equipo multidisciplinar.

DIAGNÓSTICO

El motivo de consulta más frecuente es la autopalpación de una masa mamaria. El diagnóstico en esta situación está dificultado por:

- El aumento de tamaño de la glándula mamaria durante la gestación
- El aumento de densidad mamaria durante la gestación
- La menor sospecha por parte de médico y paciente

Por ello, **toda masa palpable que persista más de dos semanas en una paciente embarazada debe investigarse mediante punción y/o biopsia** (aunque en el 80 % de los casos sean lesiones benignas). El patólogo debe saber que se trata de la muestra de una gestante.

La evaluación de la paciente embarazada con sospecha de neoplasia de mama debe incluir la exploración mamaria y de las adenopatías regionales.

La mamografía con protección abdominal se puede realizar con seguridad y es la exploración radiológica de elección. La ecografía, sin riesgo de irradiación fetal, es útil para completar la estadificación de mama y axila.

La resonancia magnética deberá evitarse durante el embarazo, ya que hay datos de que el uso del gadolinio atraviesa la placenta.

El estudio de extensión debe adaptarse minimizando la exposición del feto a la radiación. Así:

- En caso de tumores T1-2 N0, se recomienda realizar una analítica general con función renal y hepática, y radiografía de tórax.
- \geq T3 o afectación ganglionar, se recomienda añadir a las exploraciones anteriores ecografía abdominal, y resonancia magnética nuclear sin contraste de tórax y/o columna según sospecha clínica y si va a implicar cambios en el manejo terapéutico.

El cáncer de mama en el embarazo se asocia a tumores más grandes y con más afectación ganglionar (53-71 %) que en las pacientes de la misma edad no embarazadas (534).

Las características histológicas son similares a las pacientes no embarazadas de menos de 30 años. En un 70-100 % serán carcinomas de tipo ductal y, más frecuentemente, con características de agresividad (grado III en un 40-95 %, invasión linfovascular, receptores hormonales negativos y HER2 positivo según las series de hasta 30-40 % (535).



¿Cómo se trata?

TRATAMIENTO

La decisión del tratamiento requiere de un equipo multidisciplinar (ginecología, obstetricia, cirugía, oncología) para la toma de decisiones, que se basará en dos cuestiones: la primera será sobre la continuación o no del embarazo, la segunda sobre la secuencia temporal del tratamiento.

Por otra parte, se requerirá de una consulta de medicina materno-fetal y de la revisión de los riesgos maternos. La documentación del crecimiento y desarrollo del feto y de la edad del feto a través de la evaluación ecográfica es apropiada.

Cirugía

La cirugía de la mama y de la axila puede realizarse con seguridad en cualquier trimestre del embarazo.

En cuanto a la cirugía de la mama, las opciones son:

- Mastectomía radical modificada: en las primeras series era la técnica de elección. Una ventaja es que no requiere de radioterapia posterior, la reconstrucción debe posponerse a después del embarazo.
- Cirugía conservadora: su uso no parece tener un impacto negativo en la enfermedad. De hacerse, la radioterapia se debe retrasar hasta el periodo posparto. Se puede realizar sin problemas en el tercer trimestre, y valorar en función de cada caso en el primer y segundo trimestres (536, 537).

En cuanto a la cirugía de la axila, el tratamiento más aceptado es la linfadenectomía axilar. Aunque hay un número limitado de casos aislados y pequeños estudios retrospectivos que evaluaron el uso de la biopsia de ganglio centinela en pacientes embarazadas, la sensibilidad y especificidad del procedimiento no se han establecido (538, 539). Las decisiones relacionadas con el uso de la biopsia de ganglio centinela en el embarazo deben ser individualizadas. En caso de realizarse, debe minimizarse la dosis de radiación fetal con respecto al uso del trazador radioactivo, y no debe recomendarse en gestantes de menos de 30 semanas.

Quimioterapia, terapia biológica, terapia endocrina y radioterapia

Quimioterapia

Las indicaciones de la quimioterapia sistémica son las mismas en la paciente embarazada que en la paciente con cáncer de mama que no esté embarazada, a pesar de que la quimioterapia no se debe administrar nunca durante el primer trimestre del embarazo; siempre a partir del segundo trimestre (semana 14).

Se recomienda administrar esquemas de quimioterapia lo más parecidos posible a los de las pacientes no embarazadas. El cálculo de dosis de quimioterapia debe hacerse a partir del peso actual, y adaptarse en cada ciclo a los cambios de peso durante el embarazo. Se pueden utilizar fármacos como el ondansetrón, el lorazepam y la dexametasona como parte del régimen antiemético antes de la quimioterapia.

La mayor experiencia durante el embarazo es con antraciclinas y agentes alquilantes. Los datos de un estudio prospectivo de una sola institución (MDA Anderson) indican que FAC (5-FU 500 días mg/m² intravenoso 1 y 4, adriamicina 50 mg/ m² por infusión intravenosa durante 72 horas, y ciclofosfamida 500 mg/ m² intravenoso el día 1) puede administrarse con seguridad durante el segundo y tercer trimestres del embarazo. La mediana de edad gestacional al momento del parto fue de 38 semanas; más del 50 % de las pacientes tuvieron un parto vaginal, y no hubo muertes fetales (540).

Una actualización de esta experiencia informó sobre 57 mujeres tratadas con FAC en el adyuvante o neoadyuvante. Había 57 niños nacidos vivos. Una encuesta a los padres/ tutores informó sobre la salud de 40 niños. Había un niño con síndrome de Down y otros dos con anomalías congénitas (pie zambo, reflujo ureteral bilateral) (541).

Existen datos limitados sobre el uso de taxanos durante el embarazo (542, 543). Si se utilizan, se recomienda la administración semanal de paclitaxel después del primer trimestre si está clínicamente indicado por el estado de la enfermedad.

Si se inicia la terapia sistémica, la monitorización fetal antes de cada ciclo de quimioterapia es la adecuada. La quimioterapia durante el embarazo no se debe administrar después de la semana 35 del embarazo o dentro de las tres semanas previas a la fecha planificada de parto, con el fin de evitar la posibilidad de complicaciones hematológicas durante el parto.

Tratamientos biológicos

Solo existen datos de casos descritos de uso de trastuzumab durante el embarazo. La mayoría de estos informes de casos indicaron oligo- o anhidramnios con la administración del trastuzumab; en un caso se presentó insuficiencia renal fetal. Por ello, se recomienda evitar su uso durante el embarazo, ya que el receptor HER2 está implicado en la organogénesis fetal, y su uso también se ha asociado a oligohidramnios con riesgo de insuficiencia renal fetal. (544-546). Además, la lactancia materna está contraindicada debido a la transmisión del fármaco en la leche materna (547).

La misma contraindicación puede aplicarse a otros agentes antiHER2 como son Pertuzumab y TDM1. Con respecto a Lapatinib, la ausencia de experiencia hace no respaldar su uso (548).

Otros

No se recomienda el uso durante el embarazo de bifosfonatos ni nuevos fármacos (antiangiogénicos, inhibidores de tirosina quinasa, factores estimulantes de colonias).

Radioterapia y hormonoterapia

La terapia endocrina y la radioterapia están contraindicadas durante el embarazo por teratogénesis.

En definitiva, **el cáncer de mama puede tratarse durante el embarazo, siendo la cirugía y la quimioterapia posibles y seguras**. Será imprescindible definir la estrategia terapéutica por un equipo multidisciplinar.

D. ENFERMEDAD DE PAGET

¿Qué es la enfermedad de Paget y cuál es su forma de presentación?

¿Cuál es su tratamiento?

VER RESUMEN

7. Situaciones especiales
d) Enfermedad de Paget



¿Qué es la enfermedad de Paget y cuál es su forma de presentación?

INCIDENCIA, PRESENTACIÓN Y DIAGNÓSTICO

La enfermedad de Paget de la mama se caracteriza por la presencia de células neoplásicas en la epidermis del complejo areola-pezones. El cáncer generalmente afecta a los conductos del pezón primero (conductos galactóforos), y luego se extiende a la superficie del pezón y la areola. Se trata de una entidad poco frecuente, suponiendo un 1-4 % de todos los cánceres de mama (549).

Clínicamente, se caracteriza por la aparición de cambios en el pezón y la areola de la mama afecta, como son eccema de la areola, sangrado, ulceración y escozor en el pezón.

En un 80-90 % de los casos, se asocia a una neoplasia subyacente en la mama, ya sea *in situ* o infiltrante (550, 551).

Ante la sospecha clínica de una enfermedad de Paget, se debe realizar una biopsia quirúrgica incluyendo el espesor de la epidermis, así como un examen físico y radiológico de la mama. Se recomienda incluir la resonancia magnética en el estudio radiológico.

¿Cuál es su tratamiento?

TRATAMIENTO

Existen diversas opciones en cuanto al tratamiento quirúrgico:

1. Mastectomía. Tradicionalmente, la mastectomía con vaciamiento ganglionar ha sido el tratamiento más habitual
2. Cirugía conservadora incluyendo el complejo areola-pezones, seguida de radioterapia complementaria
3. Siempre debe realizarse la resección del tumor subyacente

El estudio ganglionar mediante ganglio centinela no es necesario en caso de enfermedad de Paget sin carcinoma subyacente o asociado a un carcinoma *in situ*, sin evidencia de cáncer invasivo. Dos estudios retrospectivos han proporcionado evidencia de un alto grado de precisión en la identificación del ganglio centinela en pacientes con enfermedad de Paget (552, 553).

La quimioterapia, la hormonoterapia y/o los tratamientos biológicos deben administrarse de acuerdo con el estadio y las características del cáncer de mama asociado a la enfermedad de Paget. [Capítulo 4](#)

E. TUMOR PRIMARIO OCULTO CON ADENOPATÍAS AXILARES

¿Cómo se diagnostica el tumor primario oculto con adenopatías axilares?

¿Cuál es su tratamiento?

VER RESUMEN

7. Situaciones especiales
e) Tumor primario oculto con adenopatías axilares



¿Cómo se diagnostica el tumor primario oculto con adenopatías axilares?

INCIDENCIA, PRESENTACIÓN Y DIAGNÓSTICO

El tumor primario oculto de mama con adenopatías axilares es una entidad poco frecuente; por ello, la evidencia para tratar estos casos procede de la experiencia de series retrospectivas (461, 554, 555).

La epidemiología, biología y evolución de los pacientes afectos de esta entidad, son similares a las de los pacientes con un cáncer de mama con afectación axilar. En los pacientes suelen presentarse tras una biopsia inicial. Ante la sospecha de origen mamario, es necesaria la realización por inmunohistoquímica de los RH y el HER2, así como la realización de una mamografía y ecografía mamarias. En caso de no existir evidencia de enfermedad mamaria por exploración física y mamografía, la resonancia magnética permite identificar el primario de mama en algunos casos, hasta en un 50-70 % en algunas series (554).

Se recomienda también descartar la presencia de metástasis a distancia.



¿Cuál es su tratamiento?

TRATAMIENTO

Aquellas pacientes con resonancia magnética mamaria positiva recibirán tratamiento de acuerdo con el estadio del cáncer de mama. Pero en aquellos casos en los que finalmente no se encuentre primario, pese a haberse realizado resonancia magnética, las opciones de tratamiento incluyen:

- la mastectomía con vaciamiento ganglionar axilar, o
- el vaciamiento ganglionar axilar (sin cirugía mamaria) con radioterapia mamaria con o sin radioterapia en cadenas ganglionares (554, 555).

En la práctica clínica, en caso de conservar la mama y tratarse únicamente con radioterapia, se aconseja realizar seguimiento de las mismas características que el seguimiento que se realiza a las pacientes que han sido intervenidas de un cáncer de mama (es decir, mamografía anual, etc.).

La quimioterapia, la hormonoterapia o los tratamientos biológicos se administrarán según las recomendaciones del estadio de la enfermedad y el subtipo de enfermedad.

F. PACIENTE ANCIANA

¿Cuál es la incidencia del cáncer de mama en mujeres ancianas?

¿En qué consiste la valoración geriátrica integral? ¿Cómo debe abordarse su tratamiento?

INCIDENCIA, VALORACIÓN GERIÁTRICA INTEGRAL Y ABORDAJE TERAPÉUTICO

VER RESUMEN

7. Situaciones especiales

f) Paciente anciana



¿Cuál es la incidencia del cáncer de mama en mujeres ancianas?

El cáncer de mama es una enfermedad asociada a la edad. La edad media al diagnóstico es de 61 años, y la mediana de edad de la mortalidad por cáncer de mama es de 69 años (556). En nuestra sociedad, el número de adultas ancianas con cáncer de mama y el de supervivientes de cáncer de mama se están incrementando.

¿En qué consiste la valoración geriátrica integral? ¿Cómo debe abordarse su tratamiento?

En el caso del cáncer de mama en pacientes ancianas, existirán otros factores, además de la edad cronológica, que influirán en las decisiones del tratamiento. Estos factores constituyen la valoración geriátrica integral e incluyen:

- Estado funcional: evaluación de la independencia en actividades básicas e instrumentales de la vida diaria (índice de Barthel y de Lawton).
- Comorbilidades médicas. Índice de comorbilidades de Charlson.
- Evaluación socioeconómica: accesibilidad desde su vivienda a servicios sanitarios, redes de apoyo familiar, entre otros.
- Estado nutricional: instrumento *Mini Nutritional Assessment* (MNA).
- Estado cognitivo: instrumento de Folstein: *Mini-Mental State Examination* (MMSE).
- Síndromes geriátricos: escala de depresión geriátrica de Yesavage, SPPB y velocidad de la marcha en caídas recurrentes; alteraciones del sueño, incontinencia.

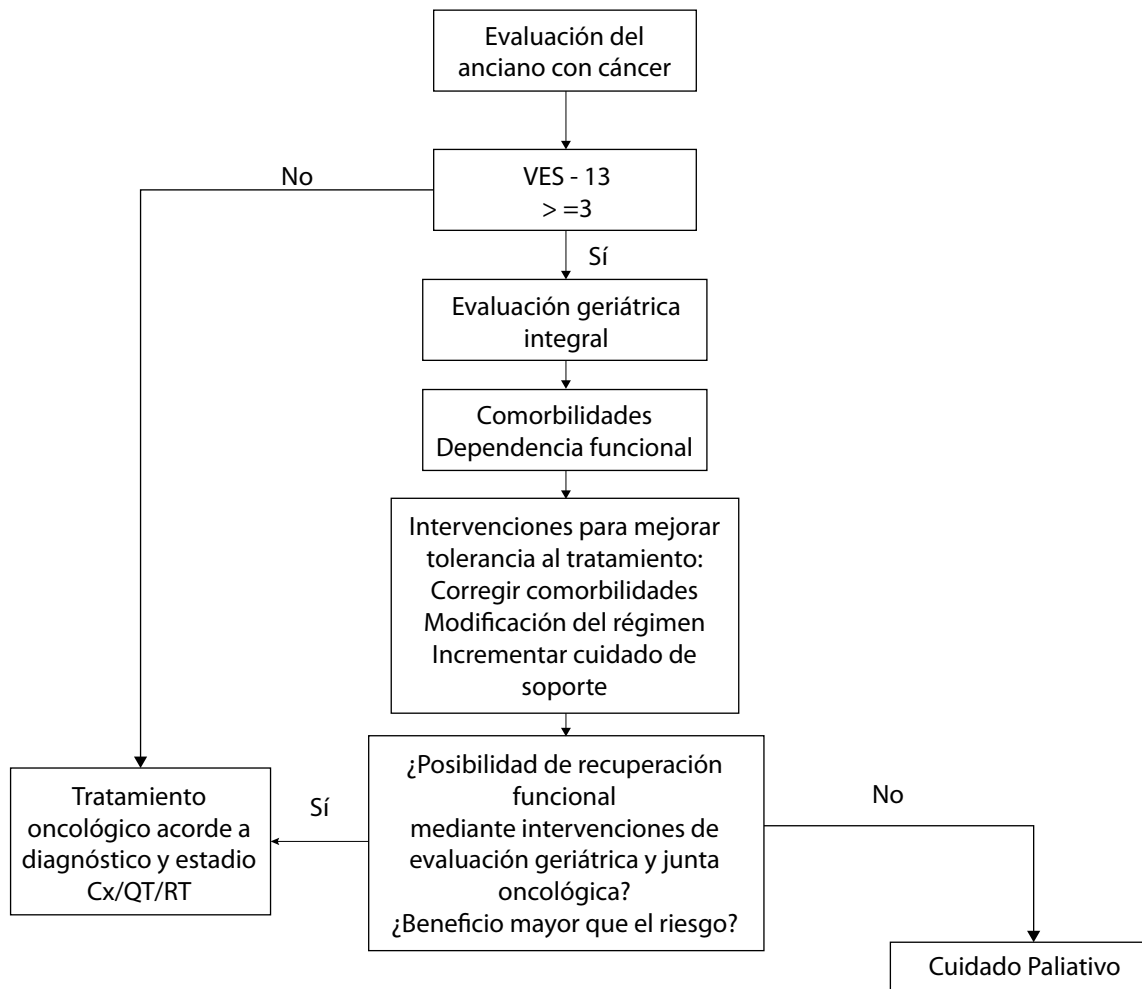
Las guías de la NCCN recomiendan que todo paciente oncológico mayor de 70 años reciba una valoración geriátrica integral, o por lo menos se le aplique una escala como el **VES-13** (*Vulnerable Elders Survey*, en la Tabla 88), **para determinar qué pacientes deben ser sometidas a una evaluación rigurosa** para la toma de decisiones en su tratamiento oncológico (557, 558).

Tabla 88. Vulnerable Elders Survey 13 (VES-13). *Basada en Rockwood K. et al., Cadena M. O. et al. (559, 560).*

Elemento de evaluación	Puntaje
Edad	
75-84 años	1
≥ 85años	3
Autopercepción del estado de salud	
Bueno o excelente	0
Regular o malo	1
Actividades básicas e instrumentales de la vida diaria	
¿Necesita ayuda para?	
Ir de compras	1
Utilizar dinero	1
Realizar trabajos ligeros en casa	1
Transportarse	1
Bañarse	1
Actividades adicionales	
¿Necesita ayuda para?	
Agacharse, ponerse en cuclillas o de rodillas	1

En definitiva, la paciente anciana requiere un abordaje integral atendiendo a toda su complejidad, y si puede ser, debe valorarse en una unidad geriátrica. Cadena M. O. et al. proponen el siguiente algoritmo en la Figura 38 (560).

Figura 38. Algoritmo de valoración de pacientes ancianos con cáncer. *Basada en Cadena M.O. et al. (560)*



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