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A unique surgical case of giant invasive intracystic carcinoma of the male breast focusing on cytological findings

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Abstract

A 60-year-old male presented with a history of a relatively hard and cystic right chest mass that had gradually increased in size, with subsequent skin erosion, exudate and hemorrhage. The cytologic specimens from a cyst fluid contained a large number of sheet-like or papillary clusters of atypical cuboidal to columnar epithelial cells with loss of myoepithelial components, in a severely inflammatory background with scattered siderophages. We first interpreted it as a carcinoma, but could not completely exclude out the possibilities of benign. Tumor extirpation was performed, and a gross examination of the neoplasm revealed a giant, cystic and partly solid papillary-projected tumor lesion, with a gray-whitish cut surface, associated focally with skin invasion, measuring approximately 9×7 cm with a 6×4 cm solid area in diameter. On a microscopic examination, solid parts of the tumor were predominantly composed of the intracystic proliferation of mildly atypical epithelial cells with absence of two-cell patterns in a papillary or papillotubular growth fashion, only partly involving the dermis to epidermis. Immunohistochemistry showed that the carcinoma cells were specifically positive for estrogen and progesterone receptors, whereas negative for p63, S-100 protein and several neuroendocrine markers. Therefore, we finally made a diagnosis of invasive intracystic carcinoma of the male breast. We should be aware that owing to its characteristic cytological features, cytopathologists might be able to make a correct diagnosis of that, based on multiple and adequate samplings, even though a core biopsy would be the absolute minimum assessment.

Keywords

Intracystic carcinoma (IC), invasive, male, breast, cytopathology

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Introduction

Intracystic carcinoma (IC) is rare among female breast neoplasms, accounting for less than 1% of all cases.[1] By contrast, although male breast carcinoma is very rare, annually one per 10,000, male IC shows a relatively higher incidence ranging from 2% to 3% of all male breast malignancy.[2,3] It is very interesting that the majority of reported cases of male IC originate from Japan, from 1983, by Noguchi et al.,[4] to 2018, by Kinoshita et al.,[5] and our present brief report. However, its backgrounds remain to be elucidated.

IC of the male breast is considered as the malignant counterpart of benign intracystic papilloma, displaying a two-cell pattern with myoepithelial components.[1–3] It often poses a diagnostic challenge to all clinicians and cytopathologists, since its entity is very difficult to diagnose pre-operatively on small, inadequate samples even from the male breast. Indeed, most of cystic breast tumors usually results in paucicellular cytological specimens with a small number of degenerative and poorly preserved carcinoma cells.[6] Furthermore, although patients with IC tend to show very

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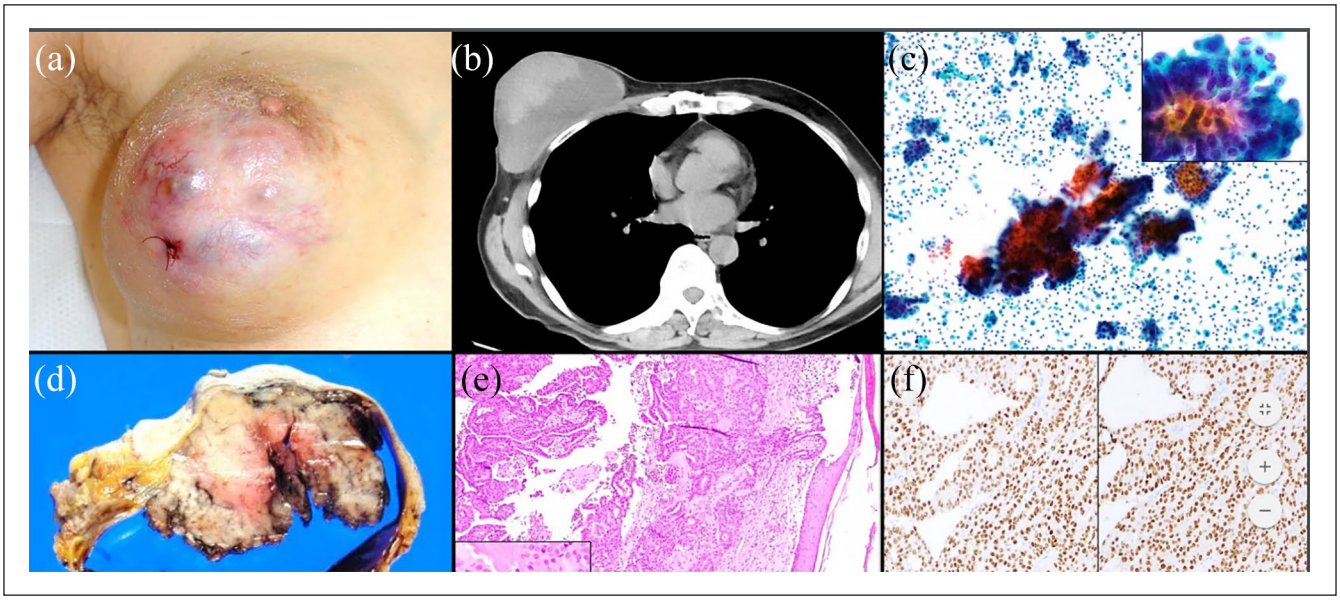

Figure 1. The findings of gross, chest CT, FNA cytomorphologic and microscopic examinations of the giant male invasive IC specimens. (a) A 60-year-old male patient incidentally has a chief complaint of a gradual increase in size of a relatively hard and cystic right chest mass with subsequent skin erosion, exudate and hemorrhage for 2 years. The chest skin below the right nipple looks markedly swelling, tense and reddish. (b) Chest CT shows a huge, partly solid and cystic, and relatively well-demarcated tumor mass with upper high-density and bottom low-density area, measuring approximately 11 × 8 cm with a 7 × 4 cm solid part in diameter, arising from the right breast. (c) The FNA cytology specimen (Papanicolaou staining) contains a large number of small to large, sheet-like or papillary three-dimensional clusters of viable and atypical cuboidal to columnar epithelial cells (inset) with loss of myoepithelial components, in a severely inflammatory background with scattered siderophages. Original magnification: 200× (inset, 400×). (d) A gross examination from the surgical specimen shows a cystic and partly solid papillary-projected tumor lesion, with a gray-whitish cut surface, associated focally with skin invasion, measuring approximately 9 × 7 cm with a 6 × 4 cm solid area in diameter. Bar = 1 cm. (e) Microscopically, the solid parts of this tumor are predominantly composed of the intracystic proliferation of mildly atypical epithelial cells with absence of two-cell patterns in an exophytic and papillary or papillotubular growth fashion. These neoplastic cuboido-columnar cells have small to medium-sized, mildly hyperchromatic and enlarged nuclei, conspicuous nucleoli and abundant eosinophilic cytoplasm, arranged in microtubular or microcystic structures filled with eosinophilic proteinaceous materials (inset). Furthermore, these tumor nests only partly invade the dermis to epidermis (upper right). Bar = 100 μm. (f) Immunohistochemical findings show that those carcinoma cells are specifically and diffusely positive for estrogen receptor (ER) (left) and progesterone receptor (PgR) or p63 (lt.) and cytokeratins, including AE1/AE3 (rt.). Original magnification: 200×.

good prognoses with 100% 10-year survival rate and 77% disease-free survival rate, respectively, overall survival for male IC seems to be lower than that for female.[7–9] Therefore, an early accurate diagnosis and surgical treatment for the male IC should allow for an improved quality of life and improved survival rates. However, there have not been many reports describing the detailed cytological features of male IC on fine needle aspiration (FNA) specimens.

Our purpose is to report an extremely rare case of male giant invasive IC originated from the right breast focusing on its cytological findings. Male IC potentially renders conclusive diagnosis possible on fully adequate and large FNA cytology specimens, even though a core biopsy would be the absolute minimum assessment.

Case presentation

A 60-year-old male patient with an unremarkable previous medical history, except for one family history of his mother's breast cancer, incidentally had a chief complaint of a gradual increase in size of a relatively hard and cystic right chest mass with subsequent skin erosion, exudate and hemorrhage (Figure 1(a)) for 2 years. The chest skin below the right nipple looked markedly swelling, tense and reddish (Figure 1(a)). Laboratory data, including blood cell count, blood chemistry and tumor markers, were within normal limits. Chest computed tomography (CT) showed a huge, partly solid and cystic, and relatively well-demarcated tumor mass with upper high-density and bottom low-density area, measuring approximately 11 × 8 cm with a 7 × 4 cm solid part in diameter, arising from the right breast (Figure 1(b)). Full-body CT revealed no definite evidence of metastases or neoplastic foci in the lymph nodes or other organs. The specimen of the FNA cytology sample from the cyst fluid (Figure 1(c)) unexpectedly contained a large number of small to large, sheet-like or papillary three-dimensional clusters of viable and atypical cuboidal to columnar epithelial cells with loss of myoepithelial components, in a severely inflammatory background with scattered hemosiderin-pigmented macrophages (i.e. siderophages) on Papanicolaou stain (Figure 1(c)). Fibrovascular cores of those

clusters were not evident, and there was no definite evidence of a necrotic background. Giemsa staining also identified very few microcalcificated materials. We first interpreted this picture as indicating carcinoma, suggestive of IC of the male breast, but could not completely exclude out the possibilities of benign tumors, including breast intracystic papilloma or skin solid-cystic/nodular hidradenoma. Tumor extirpation was thus performed, and a gross examination of the giant tumor revealed a cystic and partly solid papillary-projected tumor lesion, with a gray-whitish cut surface, associated focally with skin invasion, measuring approximately 9×7 cm with a 6×4 cm solid area in diameter (Figure 1(d)). The intracystic component contained a large volume of hemorrhagic and dark fluid. Resection was deemed most likely to be complete by this histopathological examination.

Microscopically, the solid parts of the tumor were predominantly composed of the intracystic proliferation of mildly atypical epithelial cells with absence of two-cell patterns in an exophytic and papillary or papillotubular growth fashion (Figure 1(e)). On a high-power view, these neoplastic cuboidocolumnar cells had small to medium-sized, mildly hyperchromatic and enlarged nuclei, conspicuous nucleoli, and abundant eosinophilic cytoplasm, arranged in microtubular or microcystic structures filled with eosinophilic proteinaceous materials (Figure 1(e)). Mitotic figures were rarely encountered. Furthermore, these tumor nests only partly invaded the dermis to epidermis (Figure 1(e)), indicating that they were malignant carcinomatous foci. Immunohistochemical findings showed that the carcinoma cells were specifically and diffusely positive for estrogen receptor (ER) (Figure 1(f)) and progesterone receptor (PgR) (Figure 1(f)), whereas they were negative for cytokeratin 5/6, S-100 protein, p63, thyroid transcription factor-1, CEA, chromogranin A, synaptophysin and HER2/ErbB2. The Ki67 (MIB-1) labeling index was low, approximately 2%, in those atypical cells of the tumor nests. Periodic acid-Schiff stain was not reactive for the carcinoma cells.

Based on these features, we ultimately made a diagnosis of giant invasive IC arising from the male breast. To date, we have completed approximately one year of routine follow-up since the surgery, and the patient remains well without recurrences or metastases.

Discussion

Although the overall biological behavior of ICs of the breast is generally good, aggressive surgical treatment is the gold standard for a better prognosis.[1–3,6–9] In fact, overall survival for male IC could be lower than that for female.[1–3] Thus, it might be critical to establish an accurate pre-operative diagnosis by FNA cytology, which has commonly shown a good clinical utility for diagnosing any breast tumors. However, the cytological features of male ICs have rarely been described in detail in the published literatures, due to the inadequateness and/or the rarity of this lesions.[1–3,6] To the best of our knowledge, this is the first case report of male giant invasive IC, with a focus on its cytomorphologic findings. In that sense, the present brief case report potentially interests the scientific community, even though there might not be many specific descriptions about the current case. Nevertheless, since any male patients showing a hard breast mass with skin erosion, including our case, would have a presumptive diagnosis of malignancy, such lesions need to be completely excised for treatment and diagnosis.

The cytological features of breast ICs can more or less reflect the histopathological ones; however, the false-negative rates for ICs reportedly have been relatively high, between 20% and 40%.[6] Moreover, those might be typically diverse often lacking obviously malignant characteristics.[6] FNA of ICs could cytologically show small to sometimes large, three-dimensional papillary clusters or single columnar cells occasionally with the fibrovascular cores.[6] These tumor clusters and/or columnar cells display the presence or absence of apparent nuclear hyperchromatism and pleomorphism, prominent nucleoli or mitotic figures, often without any evidence of necrotic foci.[6] In this context, intracystic papilloma must be included in the differential diagnoses of IC; however, its cytologic features are considered to reveal a two-cell pattern with apparent presence of myoepithelial components.[6] Furthermore, skin solid-cystic/nodular hidradenoma is another important differential diagnosis, but its cytology findings seem to show bimodal population of cuboidal epithelial cells having relatively abundant light-green cytoplasm, and a small number of small myoepithelial-like cells, forming sheet-like and modestly "three dimensional" clusters.[10] As in the present case, since the specimens were fully adequate, the cytologic features were very similar to those of IC, as described above, even though single columnar cells or fibrovascular cores were very rarely encountered. Thus, a conclusive and accurate diagnosis of male IC, after distinguishing from intracystic papilloma and skin solid-cystic/nodular hidradenoma, based on cytology alone, should be possible to achieve. Nevertheless, in any cases with a strong clinical suspicion of malignant male breast tumors, multiple rounds of ultrasound-guided (if possible) FNA cytology should be performed and that suspicion should be raised to alert the cytopathologists, at the very least. Finally, the findings of the current immunohistochemical analyses can suggest that immunostaining for specific myoepithelial markers, such as cytokeratin 5/6, S-100 protein and p63, and specific hormone receptor markers, such as ER and PgR, on cytological smears or cell block preparations might be useful for the differential diagnosis with intracystic papilloma or skin solid-cystic/nodular hidradenoma.

Conclusion

We encountered a very important case of male giant invasive IC arising from the right breast, tentatively diagnosed as a carcinoma, suggestive of male IC, on the examination of adequate FNA samples cytology. All cytopathologists should be aware that not only the clinicopathologically characteristic features, but also multiple, adequate FNA

specimens, might be able to lead to a correct and conclusive diagnosis, even though a core biopsy would be the absolute minimum assessment. Further cytomoprphological studies with the collection and examination of a larger number of IC cases will be required to determine whether or not cytology specimens alone can distinguish IC from other important benign breast and skin tumors.

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Ethical approval

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Data availability

The dataset supporting the findings and conclusions of this case report is included within the article.

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