ORIGINAL RESEARCH PAPER

Pathology

IMMATURE OVARIAN TERATOMA ASSOCIATED WITH GLIOMATOSIS PERITONEI AND LYMPH NODE METASTASIS: A RARE CASE REPORT AND REVIEW OF LITERATURE

KEY WORDS: Immature teratoma; gliomatosis peritonei; lymph node

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ABSTRACT

Immature teratomas are rare tumours occurring mainly in children and young adults. We report our experience with a 34 year old lady with immature teratoma with multiple glial implants in omentum, gliomatosis peritonei and pelvic lymph node. Immature teratoma has to be differentiated from a mature teratoma which is based on the presence of immature neuroepithelium. Gliomatosis peritonei is an interesting condition in which immature and mature teratomas become associated with a myriad of peritoneal nodular or miliary implants composed of mature glia. It is important to grade any peritoneal or lymphnode deposit which may adversely affect the overall stage of the tumour. In this case report we have briefly discussed the various aspects of this tumour. A total of nine cases with glial tissue in lymph node i.e nodal gliomatosis have been published previously with or without in association with GP.

INTRODUCTION

Teratomas are the most common germ cell tumour of ovary. They are represented as mature and immature according to the presence of immature embryonal elements particularly neural in immature teratoma or a teratoma can have a large component of a single endodermal or ectodermal type of tissue or is composed exclusively of such tissue. This type of teratoma is known as a monodemal teratoma.[1]

Immature teratoma (IT) is a preferred term for the malignant ovarian teratoma. It is more common in children and adolescents and is composed of a mixture of embryonal and adult tissues derived from all three germ layers.[2] According to WHO, IT is defined as a teratoma containing a variable amount of immature embryonal type (generally) neuroectodermal tissue.[3] These tumours are graded according to the amount of neural epithelium present. Therefore a thorough and extensive sampling of the ovary is required so that such areas are not missed.

Extraovarian spread usually takes the form of peritoneal implants, liver and lung nodules and less often lymphatic or hematogenous metastases.[1] Such implants mainly are composed mainly of mature glial tissue and don't adversely affect the prognosis. The implantation in the peritoneum of mature glial tissue is known as gliomatosis peritonei. Lymph node metastasis with mature glial tissue in combination with gliomatosis peritonei is very rarely reported.

Because of its rarity, we report our experience with a 34 year old lady with a 4500 gm mass presenting with pain abdomen. This case is intended to identify and study about this rare neoplasm with an unusual age of presentation in this woman.

CASE REPORT

A 34 year old female came to outpatient department of Obstetrics and Gynecology of VMMC and Safdarjung hospital, New Delhi with a history of abdominal pain and increase in abdominal volume of 5-6 months duration. She had an unremarkable family history. An USG was ordered which showed a large abdomino-pelvic mass arising from the ovary measuring 25X21cm. Pelvic lymphadenopathy was observed without any liver involvement. Following this the tumour was removed for suspected malignancy and the histopathology sample was sent to the department of pathology, VMMC and Safdarjung hospital, New Delhi.

We received a specimen of a left ovary measuring 23X20X12 cm. External surface was bosselated. On cut, the surface was gritty and we observed a multicystic tumour filled with seromucinous fluid. A few solid areas along with many cystic areas were also seen. Uterus, cervix and fallopian tube were unremarkable. We also received specimen of omentum measuring 28X18 cm. Grossly no deposits or nodules were observed. We also received 2 pelvic lymphnodes measuring 1 cm each in diameter which on cut were grey white.

The ovarian specimen was thoroughly sampled and multiple sections were taken. Section showed a tumour with a mixture of mature and immature elements. This included mature adipose tissue, cartilage, stratified squamous epithelium and glandular spaces lined by columnar cells. Areas of fibrillary neural tissue, glial tissue, ganglion cells, areas of calcification, skin and adnexal structure were also seen. A foci of woven bone was also present. Immature neural tissue was seen in the form of primitive neural tubes and rosettes(figure 1A) and immature cartilage. These histological features were suggestive of immature teratoma (Grade 1).

Sections from omentum revealed many foci of nodular mature glial tissue (Grade 0) (figure 2). Sections from the 2 pevic lymphnodes showed the presence of subcapsular deposits of mature glial tissue(figure 3). The immunohistochemistry was also performed at this time and it showed positive staining for glial fibrillary acidic protein (GFAP, monoclonal Mouse Anti-human, Biogenex) on the omental and lymphnode samples. This clearly showed the omental and lymph nodal deposits of the mature glial tissue (figure 2,3 inset).

Thus a diagnosis of immature teratoma (Grade 1) with multiple glial implants in omentum, gliomatosis peritonei (Grade 0) and pelvic lymph node (Grade 0) metastasis of mature glial tissue.

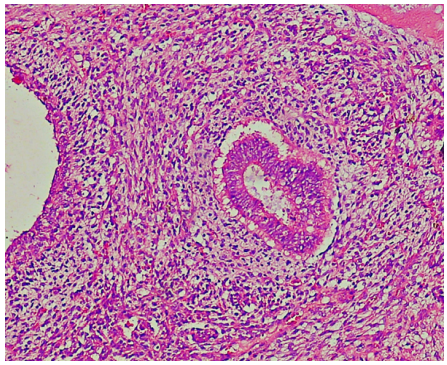

Fig 1A- Shows immature/primitive neural tissue in the form of neural tube (20X, H&E)

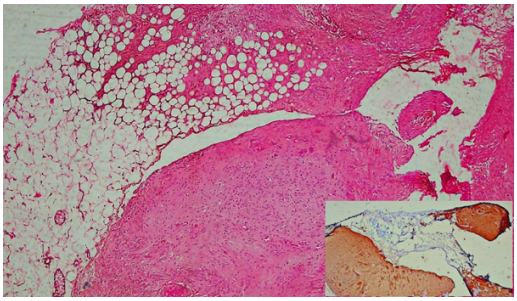

Fig 2- Deposit of mature glial tissue in omentum (40X,H&E), inset- the glial tissue in omentum was positive for GFAP (40X,monoclaonal mouse antibody, Biogenex)

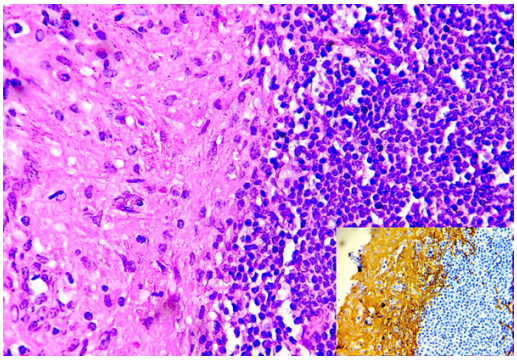

Fig 3- Lymph node metastasis of metastasis of mature glial tissue (40X,H&E) which is positive for GFAP (inset) [40X, mouse antibody, Biogenex]

DISCUSSION

Immature teratoma is a rare germ cell neoplasm of the ovary which is usually seen in children and adolescents. These tumours are composed of embryonal and adult tissue derived from all the germ layers.[2] IT comprise less than 1% of all cancers, 2% of all germ cell tumours and 10-20% of all cases encountered in first two decades of life.[1]

The histological assessment of its degree of immaturity is a highly reliable prognostic indicator.[4] Grading is performed by a subjective and a semiquantitative analysis of the relative number of foci of immature neural tissue (neuroepithelial tubules and neural blastema) present in the tumor. This is accomplished either by a 2-tier system (low grade and high grade) or by assigning 4 grades ranging from fully mature (0) to highly immature(3)[5-6]. Foci of neural tissue either mature or immature may get implanted in the peritoneum or rarely metastasize to the surrounding lymphnode. Implantation of immature tissue may adversely affect the prognosis so it has a prognostic importance to identify these implants. This is also particularly important in case of children and young adults so as to avoid unnecessary destructive procedures so as to preserve the endocrine and reproductive function.

Gliomatosis peritonei (GP) is an interesting condition in which immature and mature teratomas become associated with a myriad of peritoneal nodular or miliary implants composed of mature glia.[7] Despite its clinical stage III, mature glial cells are not aggressive and remain stable for long periods of time and behave in a benign manner. However, on rare occasions, GP can induce a florid vascular proliferation leading to massive peritoneal hemorrhage and shock.[8] Very rarely it can even undergo a malignant change to form a secondary malignant glial tumor.[9]

Multiple genetic studies has been done regarding the histogenesis of this rare phenomenon. These findings proposed a different genetic identity for ovarian tumor and GP, the latter originating from peritoneal pluripotent cells stimulated by growth factors present in the primary tumor that would induce differentiation into glial cells.[10] However according to Nogales et al, to the traditional origin for GP as a peritoneal seeding via capsular rupture from the ovarian teratoma is also supported by the following facts: (1) GP nodules often show multiple tissue differentiation (skin, gut, cartilage); (2) neural tissue itself is polydifferentiated with several neurogenic lines including microglia; (3) immature neuroepithelial tubules coexist in some cases with mature glia, indicating maturation from embryonal precursors; (4) shed hair and keratin scales from teratoma are often found associated with GP; and (5) lymph node involvement by mature glia may occur in the absence of GP.[7,12,25] In this regard further studies are required to support each of the theories and a better understanding of this phenomenon.

The use of pluoripotent markers can enhance the identification of the tissue components. This will help in better differentiation of a mature from an immature teratoma. Recently markers such as SOX2 and SALL4 are being used which are strongly expressed by immature neuroepithelium but are weaker or absent in well-differentiated neural areas.[13]It has been observed that SOX2 behaves as the more specific antibody for immature neural areas, being particularly useful in PNET overgrowths of teratoma.[13-14]

Glial tissue can also metastasize to the pelvic lymphnodes but it is rare phenomenon[1] and literature regarding the same is scant. On a detailed and extensive search of Medline /Pubmed we could only find 10 cases including the present case (Table 1). The first case was described by Benirschke *et al (1960)* in which they presented a case of a 19 year old female with mature teratoma having retroperitoneal, iliac, Cervical and axillary node gliomatosis.[21] The first case of immature tertoma with nodal gliomatosis was described by Kourie and Roujeau (1966) which was case of a 9 year old girl presenting with immature teratoma and mesenteric node gliomatosis.[22]

Sl. No.	Reference	Primary tumour with associated glial implants	Lymphnode involved by glial tissue	Age/sex	Treatment	Outcome
1	Benirschke *et al.* (1960)[21]	Ovarian mature teratoma, GP	Retroperitoneal, iliac, cervical, axillary (G0)	18/F	Chemotherapy	Dead after 8 months
2	Kourie and Roujeau (1966)[22]	Ovarian immature teratoma (G1), GP	Mesenteric (G1)	9/F	No further treatment	No recurrence
3	Robboy and Scully (1970)[23]	Ovarian immature teratoma (G1), omentum, GP	Mesenteric (G1)	9/F	No further treatment	No recurrence
4	Nagashima *et al.* (1974)[24]	Ovarian immature teratoma, pleural gliomatosis	Inguinal, mesenteric, mediastinal, cervical	22/F	Chemotherapy	Dead after 8 months
5	Perrone *et al.* (1986)[25]	Ovarian immature teratoma (G1)	Para-aortic (G0)	10/F	No further treatment	No recurrence
6	El Shafie *et al.* (1984)[15]	Ovarian teratoma, serosa of small and large intestine, appendiceal surface, GP	Omental (G0)	12/F	No further treatment	No recurrence
7	Harms *et al.* (1989)[26]	Ovarian immature teratoma (G1), GP, hepatic serosa	Para-aortic (G3)	13/F	Chemotherapy	No recurrence
8	Khan *et al.* (2005)[27]	Ovarian immature teratoma (G1), omentum, GP	Lymph node (G0)	23/F	Chemotherapy	Not described
9	Kim *et al.* (2013)[28]	Ovarian immature teratoma (G1), GP	Hypogastric (G0)	34/F	No further treatment	No recurrence
10	Bhuyan et al (present case)	immature teratoma (G1) omentum, GP	Pelvic(G0)	34/F	No further treatment	No recurrence

Table 1- Review of cases of ovarian teratoma with gliomatosis peritonei and lymph node metastasis

In this case we used Glial fibrillary acidic protein (GFAP) which is an 52kD intermediate filament protein that expresses with the development of astrocytes in the fetal nerve tissue. In our case we found stong immunoreactivity with GFAP which suggests the matue and well differentiated nature of the neural tissue.

The treatment of IT with GP and lymph node metastasis is complete surgical resection preventing the malignant transformation of the GP or lymph node deposits. However in extensive lesions complete surgical excision may not be possible. This requires careful radiological monitoring and regular follow-ups of the patient to prevent any recurrences. In such cases the use of cisplatinum based chemotherapy typically with bleomycin, etoposide and cisplatin is advised.[17] This can bring about the conversion of the metastatic immature teratoma into a mature teratoma the phenomenon which in known as growing teratoma syndrome. Growing teratoma syndrome (GTS) is a rare clinical entity, which presents with enlarging teratomas masses of the retroperitoneum or other locations, occurring during or after systemic chemotherapy for the treatment of nonseminomatous germ cell of the testis (NSGCT), with normalised tumour markers.[18] This is completely benign condition and awareness of this syndrome is necessary in order to prevent unnecessary chemotherapy and allow optimal management.

The progression of IT depends on its FIGO stage [19] of the tumour. The prognosis is adversely influenced by several factors, such as tumor grade, growth pattern, capsular rupture and vascular invasion. The risk of metastasis depends on the amount of immature neural tissue present which is graded according to the system by Robboy and Scully modified by Norris et al.[20]

In conclusion we believe that it is difficult to differentiate a mature from an immature teratoma intraoperatively. The appearance of glial implants in the peritoneum doesn't warrant an extensive surgery and a more conservative approach should be taken to preserve the endocrine and reproductive function in a young female. When associated with mature glial implants within the peritoneum the prognosis is usually much better irrespective of the original tumor grade.[20] In such patients with intraperitoneal and lymph node metastases of mature glial tissue, no therapy is needed for such metastases. The prognosis in these patients is excellent, but long-term follow-up is mandatory.

In the case of our patient after 6 months of the surgery the patient has been kept under regular followup. Till date no tumour recurrence has been noted and the patient is doing well.

DECLARATION OF PATIENT CONSENT

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Nil.

CONFLICTS OF INTEREST

There are no conflicts of interest.

LEGENDS TO FIGURES

FIGURE 1(A)-

Shows immature/primitive neural tissue in the form of neural tube (20X, H&E)

FIGURE 2-

Deposit of mature glial tissue in omentum (40X,H&E), inset- the glial tissue in omentum was positive for GFAP (40X,monoclaonal mouse antibody, Biogenex)

FIGURE 3-

Lymph node metastasis of metastasis of mature glial tissue (40X,H&E) which is positive for GFAP (inset) [40X, mouse antibody, Biogenex]

TABLE 1-

Review of cases of ovarian teratoma with gliomatosis peritonei and lymph node metastasis

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