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Original Research Article

A Retrospective Study to delineate the application of SIOP protocol and evaluate its utility in pre-treated Nephrectomy specimen of Wilm's Tumor: A Pathologist's Perspective

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Abstract:

BACKGROUND: Wilms tumour, or nephroblastoma, is the most common type of kidney cancer in children, primarily affecting those aged less than 15 years. We present the histological analysis of Wilms tumour post chemotherapy according to SIOP (International society of paediatric oncology) protocol.

AIMS & OBJECTIVE:

- To evaluate the degree of tumour regression post chemotherapy and correlate it with initial tumour characteristics.
- To systematically analyse histological features of Wilms' tumour in pretreated nephrectomy specimens.
- To classify tumours based on favourable vs. unfavourable histology and assess the presence of anaplasia.

Material and Methods:

Source of data: Study was carried out in post graduate pathology department at Mahatma Gandhi Memorial Medical College and M.Y. Hospital a tertiary care centre in Indore, Madhya Pradesh.

Study design: Retrospective analysis of 20 patients from one year study from July 2023 to July 2024.

Method of collecting data: The data for this retrospective study was collected over one year .Tumour specimen received , processed and underwent with histopathological study.

Statistical study: In this cross-sectional analysis, data was gathered, tabulated and systematically examined using relevant statistical methods. Findings were then compared to previous studies.

RESULTS: A total of 20 cases were studied. Tumour samples were analysed post-chemotherapy to determine necrosis, cellularity, and presence of viable tumour and its further classification into various stages.

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CONCLUSION: Histopathological evaluation serves as a critical tool in assessing the effectiveness of preoperative chemotherapy, guiding future management, and improving patient outcomes.

1. INTRODUCTION

The SIOP protocol for treating Wilms tumour offers several advantages compared to other protocols, such as the Children's Oncology Group (COG) approach. Here are some key benefits:

1. Preoperative Chemotherapy
Reduction in Tumour Size: SIOP typically involves preoperative (neoadjuvant) chemotherapy, which can shrink tumours, making them easier to remove surgically and potentially allowing for nephron-sparing surgeries[1].
Assessment of Response: This approach helps assess the tumour's response to chemotherapy, guiding further treatment.

2. Less Invasive Surgery
3. Focus on Quality of Life
Long-Term Outcomes: By balancing aggressive treatment with the preservation of kidney function and minimizing late effects, the SIOP protocol supports better long-term quality of life for survivors[2].

4. Standardized Protocols
• **Consistency in Care**: SIOP provides standardized treatment protocols that can be adapted globally, ensuring that children receive evidence-based care regardless of location.

- **Handling of wilm’s tumour specimen**

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Orient the specimen properly by locating the hilum and identify its contents. Ink the entire outer surface of the kidney to recognize Gerota's fascia while taking tissue samples. After weighing the specimen, sample the resection margins of the ureter, renal vein and renal artery[3-5]. Open The specimen preferably through the hilar plane starting from the medial aspect continuing laterally. Wilms tumour is usually sharply demarcated, relatively spherical mass with a "pushing" border. Document the dimensions of the whole specimen and of the tumour[6].

Sections to be submitted:
a. Tumour grid
b. Tumour with renal capsule
c. Tumour with Gerota's fascia
d. Tumour with hilar structures
e. Renal sinus
f. Renal pelvis and vessels
g. Ureteric and vascular cut margins

SIOP PROTOCOL:

Wilms tumour is a heterogeneous embryonal tumour composed of blastemal, epithelial and stromal components.

Patients diagnosed with Wilms tumour are treated with chemotherapy for 4 or 6 weeks before surgery, depending on metastatic status.
Postoperatively, treatment stratification relies on overall and local stage, and also on histological classification into low-risk, intermediate-risk and high-risk Wilms tumours.

Staging according to SIOP protocol:
Stage 1 (a) Tumour is limited to kidney and is completely resected
(b) The tumour may be protruding into the pelvic system and "dipping" into the ureter (but it is not infiltrating their walls) (c) The vessels of the renal sinus are not involved (d) Intrarenal vessel involvement may be present
Stage 2 (a) The tumour extends beyond kidney or penetrates through the renal capsule and/or fibrous pseudo capsule into perirenal fat but is completely resected (b) The tumour infiltrates the renal sinus and/or invades blood and lymphatic vessels outside the renal parenchyma but is completely resected (c) The tumour infiltrates adjacent organs or vena cava but is completely resected.
Stage 3 (a) Incomplete excision of the tumour, which extends beyond the resection margins (b) Any abdominal lymph nodes are involved (c) Tumour rupture before or intraoperatively (regardless of other criteria for staging) (d) The tumor has penetrated through the peritoneal surface (e) Tumour thrombi present at resection margins of vessels or ureter, transacted or removed piecemeal by surgeon (f) The tumour has been surgically biopsied prior to preoperative chemotherapy or surgery
Stage 4 Hematogenous metastases (lung, liver, bone, brain, etc.) or lymph node metastases outside the abdominopelvic region
Stage 5 Bilateral renal tumours at diagnosis.

Histopathological Evaluation of Wilms' Tumor:
- **Tumor Type Classification**:

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- **Favorable Histology**: Characterized by triphasic differentiation (epithelial, stromal, and blastemal components) without anaplasia.
- **Unfavorable Histology**: Features anaplasia, which is associated with a poorer prognosis.

- **Tumour Grading**:
  - An assessment of tumor differentiation, including the presence of nuclear pleomorphism and the degree of anaplasia.
- **Staging**:
  - Based on the presence of local or metastatic disease, following the SIOP staging system (Stages I-V).

Histological classification of bilateral Wilms tumour - Synchronous bilateral Wilms tumours (stage V) occur in ~5% of patients, and these children are more likely to have an underlying genetic predisposition. These patients are treated with preoperative chemotherapy for 6–12 weeks and nephron-sparing surgery (NSS) is considered by the surgical panel, taking into account tumour response to chemotherapy, to spare as much renal function as possible. In children <6 months of age, immediate surgery is recommended in the UMBRELLA protocol, as opposed to preoperative chemotherapy.

- **Biopsy Protocol**:
  - Typically, a needle biopsy is avoided preoperatively. Histological diagnosis is confirmed after nephrectomy.
- **Molecular Markers**:
  - Research into several molecular markers and genetic alterations (e.g., chromosome 11p13 deletions associated with Wilms' tumour) is ongoing and may influence treatment decisions.
- **Surgical Approach**: SIOP protocols often promote less aggressive surgical interventions when possible, preserving kidney function by opting for partial nephrectomy if the tumour shrinks adequately.

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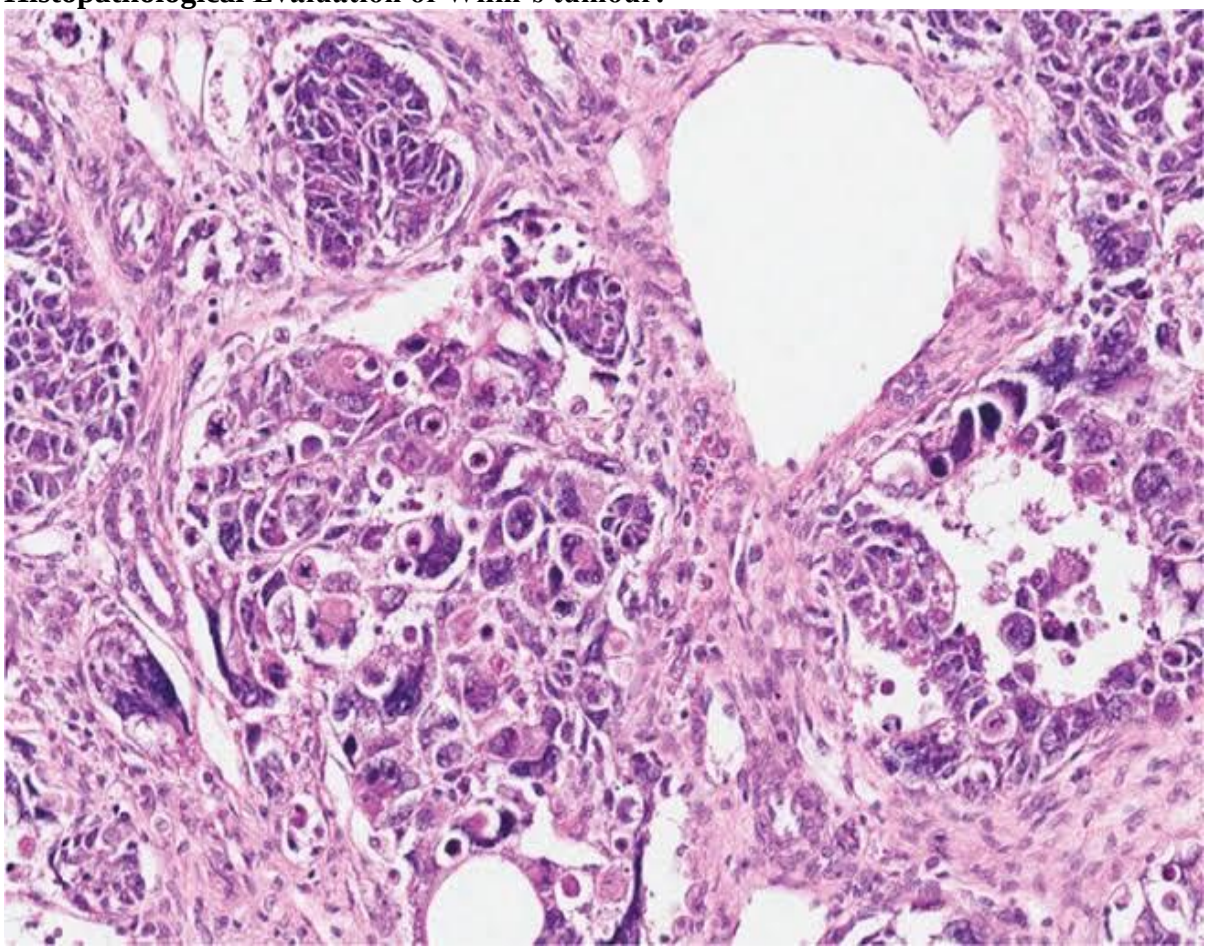
Histopathological Evaluation of Wilm's tumour:



The low-risk group includes Wilms tumours that become completely necrotic owing to preoperative treatment. Tumours in other risk groups are subclassified on the basis of viable tumour components. The intermediate-risk group includes the epithelial-type, stromal-type, mixed-type and regressive-type tumours and Wilms tumours with focal anaplasia The blastemal component consists of undifferentiated, primitive cells resembling embryonic kidney tissue. This component is usually tightly packed and has a high nuclear-to-cytoplasmic ratio. Predominantly blastemal tumours exhibit high cellularity, which can be indicative of aggressive behaviour. Architecture may appear solid, with minimal stroma or differentiation.

Table No.1: Histopathoplogical classification of Wilm's Tumour:

Tumour Type	Chemotherapy induced change	Blastema (% of viable tumour)	Epithelium (% of viable tumour)	Stroma (% of viable tumour)
Completely Necrotic	100	0	0	0
Regressive	>66	0-100	0-100	0-100
Mixed	<66	0-65	0-65	0-65
Mixed	<66	11-65	0-89	0-89
Epithelial	<66	0-10	66-100	0-33

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Stromal	<66	0-10	0-33	66-100
Blastemal	<66	66-100	0-33	0-33

2. RESULTS:

As per SIOP protocol, patients diagnosed with Wilms tumour are treated with chemotherapy for 4 or 6 weeks before surgery, depending on metastatic status we conducted a one year study among 20 post-operative Wilm's tumour cases. Age presentation was from 03 –15 years. postoperatively, treatment stratification relies mainly on histological classification, which is into low-risk, intermediate-risk and high-risk Wilms tumours Among our study ,03 cases belonged to high risk cases, 06 cases were of intermediate and 10 of them from low risk .02 cases out of 20 had bilateral tumours. 40% of all relapses occur in children whose tumour was not histologically classified as high-risk Wilms tumour, a need to improve treatment stratification is evident.

3. DISCUSSION:

Wilms tumour is a histologically heterogeneous embryonal tumour composed of blastemal, epithelial and stromal components.

In the intermediate-risk group, in addition to histological sub classification, the tumour volume after preoperative chemotherapy (measured using imaging) is of importance for treatment stratification. If the tumour volume is >500 ml in stage II/III mixed-type, regressive-type, or focal anaplasia-type tumours, these tumours are considered to have an increased risk of poor outcome and are treated aggressively[7].

The most important viable component to recognize in pretreated Wilms tumours is blastema, which is the most undifferentiated tumour component and is composed of primitive, undifferentiated cells that are arranged in no particular pattern. Blastemal-type Wilms tumour (in which >66% of the viable tumour consists of blastema in a tumour that is >33% viable) confers a worse prognosis and is, therefore, classified as a high-risk tumour according to the SIOP–2001 working classification. These blastemal-type Wilms tumours were treated with more intensive postoperative treatment than other tumour types in the SIOP–2001 trial, resulting in improved outcomes[8].

Anaplasia has been recognized as a high-risk Wilms tumour feature for many years, and it confers a worse prognosis. Anaplasia can occur in any component of Wilms tumours, and it can be focal or diffuse. Importantly, in order to diagnose anaplasia, all three criteria need to be present: mitotic figures; marked nuclear enlargement, with nuclear diameters at least three times those of adjacent cells; and hyperchromatic tumour cell nuclei[9].

Wilms tumour with focal anaplasia is regarded as an intermediate-risk tumour in the latest UMBRELLA protocol, if focal anaplasia is present in blastemal-type Wilms tumour, it is regarded as a high-risk tumour.Diffuse anaplasia is defined as nonlocalized or multifocal anaplasia, focal anaplasia with marked nuclear unrest in the rest of the tumour, or anaplasia outside of the kidney[10].

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4. CONCLUSION

This retrospective study highlights the significance of applying the SIOP (International Society of Pediatric Oncology) protocol in the evaluation of pre-treated nephrectomy specimens of Wilms tumor from a pathologist's perspective. The study demonstrates that adhering to the SIOP guidelines provides critical insights into the tumor's response to preoperative chemotherapy, as well as the prognostic implications for further treatment strategies. The findings underscore the utility of the SIOP protocol in standardizing histopathological evaluation, facilitating accurate assessment of tumor regrowth, necrosis, and residual disease, and ultimately guiding clinical decision-making. By reinforcing the importance of consistent and thorough pathological evaluation, this study advocates for its continued use in improving patient outcomes, especially in the context of pre-treated Wilms tumor cases.

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